

Oxamide IMPDH Inhibitors

Background of the Invention

5 The present invention relates to novel oxamide derivatives, a process for their manufacture, pharmaceutical preparations containing these derivatives, and the use of these derivatives as medicaments. In particular, the present invention relates to novel oxamide derivatives which are inhibitors of inosine monophosphate dehydrogenase (IMPDH).

10 Inosine monophosphate dehydrogenase (IMPDH) is an enzyme involved in the de novo synthesis of guanine nucleotides. The enzyme catalyses the NAD-dependent oxidation of inosine-5'-monophosphate (IMP) to xanthosine-5'-monophosphate which is the rate limiting step in the synthesis of guanine nucleotides. As a result of the key role of the enzyme in guanine nucleotide biosynthesis, the enzyme represents an important target for the development of inhibitors which would have utility as therapeutic agents in the treatment of
15 IMPDH related processes.

The de novo synthesis of guanine nucleotides is particularly important in B- and T-lymphocytes to provide sufficient levels of nucleotides to support a proliferative response to mitogen or antigen [Wu, J.C., Persp. in Drug Discovery and Design., 2, 185-204, (1994)].
20 IMPDH inhibition is thus an attractive target for selectively inhibiting the immune system. Inhibitors of IMPDH are known [Pankiewicz, K.W., Exp. Opin. Ther. Patents., 9, 55-65, (1999)], and the uncompetitive inhibitor mycophenolic acid (MPA) has been demonstrated to inhibit the response of B-and T-cells to mitogen or antigen [Allison, A.C. and Eugui, E.M., Transplant. Proc., 25, 8-18, (1993)]. MPA has therefore been utilised as an
25 immunosuppressant.

It is also recognised that IMPDH plays a role in other rapidly proliferating cells such as tumour cell lines, indicating that IMPDH inhibition is a target for anti-cancer chemotherapy [Nagai, M. et al., 51, 3886-3890, (1990)].

30 IMPDH inhibition has also been shown to play a role in viral replication in some cell lines which support virus replication [Pankiewicz, K.W., Exp. Opin. Ther. Patents., 9, 55-65, (1999)]. Ribavirin, for example, is a broad spectrum antiviral agent which has been approved by the U.S. Food and Drug Administration for use as an aerosol for infants with serious

respiratory infections due to respiratory syncytial virus and is also in use as an agent for the treatment of patients infected with Hepatitis C virus when used in combination with interferon [Patterson, J.L. and Fernandez-Larsson, R., Rev. Infect. Dis., 12, 1139-1146, (1990); McHutchison, J.G. et al., New. Engl. J.Med., 339, 1549-1550, (1998)]. Ribavirin is converted
5 in cells to ribavirin 5' monophosphate which is an inhibitor of IMPDH.

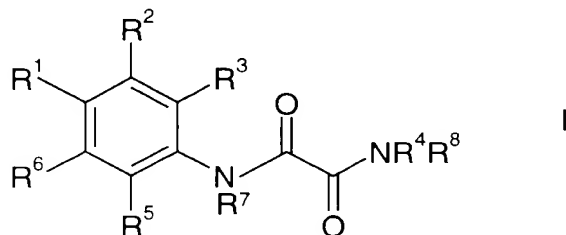
Additionally, the IMPDH inhibitors ribavirin and MPA have been shown to inhibit the replication of yellow fever virus (a RNA virus) whilst MPA has been demonstrated to inhibit Hepatitis B virus replication (a DNA virus) in vitro supporting the broad range antiviral
10 activity of these inhibitors [Neyts, J. et al., Antiviral Res., 30, 125-132, (1996); Gong, Z.J. et al., J. Viral Hepatitis., 6, 229-236, (1999)]. Furthermore, MPA has also been shown to potentiate the antiviral effects of nucleoside analogues both in vitro and in animal models [Neyts, J. and De Clercq, E., Inter. Antiviral News., 7, 134-136, (1999)]. Together these observations indicate that IMPDH inhibitors have utility as broad spectrum antiviral agents.

15

IMPDH inhibitors would therefore have therapeutic potential as immunosuppressants, anti-cancer agents and anti-viral agents. Specifically, such compounds may be used in the treatment of transplant rejection, the treatment of cancer and as antiviral agents in the treatment of viral diseases such as retroviral infections and hepatitis C virus infections (either alone or in
20 combination with other antiviral agents such as interferon or derivatives thereof, such as conjugates with polyethylene glycol).

Summary of the Invention

The novel oxamide derivatives provided by the present invention are compounds of the
25 general formula (I):



wherein

- 5 R^1 represents heterocyclyl;
 R^2 represents hydrogen, unsubstituted lower alkyl, lower alkoxy, halo, hydroxy or
 cyano;
 R^3 represents hydrogen, unsubstituted lower alkyl, lower alkoxy, halo, or cyano;
 R^4 represents hydrogen, or unsubstituted lower alkyl;
10 R^5 represents hydrogen, unsubstituted lower alkyl, lower alkoxy, halo, or cyano;
 R^6 represents hydrogen, unsubstituted lower alkyl, lower alkoxy, halo, or cyano;
 R^7 represents hydrogen, or unsubstituted lower alkyl;
 R^8 represents hydrogen, lower alkyl, lower cycloalkyl, aryl, or heterocyclyl;
 or R^4 and R^8 together with the nitrogen atom to which they are attached represent heterocyclyl;
15 and pharmaceutically acceptable salts thereof.

The oxamide derivatives provided by the present invention are inhibitors of the enzyme
inosine monophosphate dehydrogenase (IMPDH). They can be used as medicaments,
20 especially for treating immune mediated conditions or diseases, viral diseases, bacterial
 diseases, parasitic diseases, inflammation, inflammatory diseases, hyperproliferative vascular
 diseases, tumours, and cancer. They can be used alone, or in combination with other
 therapeutically active agents, for example, an immunosuppressant, a chemotherapeutic agent,
 an anti-viral agent, an antibiotic, an anti-parasitic agent, an anti-inflammatory agent, an anti-
25 fungal agent and/or an anti-vascular hyperproliferation agent.

In particular, compounds of the present invention and compositions containing the same are
useful as chemotherapeutic agents, inhibitors of viral replication and modulators of the
immune system, and can be used for the treatment of viral diseases such as retroviral infections
30 and hepatitis C virus infections (either alone or in combination with other antiviral agents
 such as interferon or derivatives thereof, such as conjugates with polyethylene glycol),
 inflammatory diseases such as osteoarthritis, acute pancreatitis, chronic pancreatitis, asthma,
 and adult respiratory distress syndrome, hyperproliferative vascular diseases such as restenosis,

stenosis and arteriosclerosis, cancer, for example lymphoma and leukaemia, and as immunosuppressants in the treatment of autoimmune diseases, graft versus host diseases and transplant rejection

- 5 Compounds of the present invention which have antiviral effects and/or immuno-suppressive properties are particularly useful for treating HCV infection.

Detailed Description of the Invention

- 10 If not otherwise specified, an unmodified term includes both substituted and unsubstituted forms if that term has been defined as substituted or unsubstituted. For example "lower alkyl" includes substituted and unsubstituted lower alkyl. Similarly, "optionally substituted" includes substituted or unsubstituted. The term "saturated" applied to ring structures includes fully and partially saturated rings.
- 15 As used herein, the term "lower alkyl", means a straight-chain or branched-chain alkyl group containing up to 10 carbon atoms, preferably from 1 to 8 carbon atoms, more preferably from 1 to 6 carbon atoms, e.g. methyl, ethyl, n-propyl, isopropyl, n-butyl, sec.butyl, tert-butyl, n-pentyl, n-hexyl and 1,1-dimethylethyl; and which is unsubstituted or substituted by e.g. one or more of cyano, halo, carboxyl, hydroxyl, lower alkoxy, lower cyclo alkoxy, aryloxy,
- 20 heterocycloxy, heterocyclyl -(lower alkoxy)-aryl-amino-oxalyl-oxy, lower alkoxy-carbonyl, aryl, aryl-carbonyl-amino-aryl, lower alkyl-carbonyl-amino-aryl, heterocyclyl, lower alkyl-heterocyclyl, lower cycloalkyl, lower alkenyl, lower alkynyl,
- 25 amino, mono- or di-(lower alkyl) amino, lower cycloalkyl amino, aryl amino, heterocyclyl-amino, lower alkyl-aryl-lower alkyl-amino, lower alkoxy-carbonyl-amino, lower alkenyl-carbonyl-amino, lower alkyl-carbonyl-amino, di-(aryl)-lower alkyl-carbonyl-amino, lower alkyl-sulphonyl-lower alkyl-carbonyl-amino, lower cycloalkyl-lower alkyl-carbonyl-amino, heterocyclyl-lower alkyl-carbonyl-amino, lower alkoxy-lower alkyl-carbonyl-amino, di-aryl-
- 30 lower alkyl-carbonyl-amino, aryl-carbonyl-amino, lower alkyl-aryl-carbonyl-amino, tri-(lower alkyl)-aryl-carbonyl-amino, mono- or di-(lower alkoxy)-aryl-carbonyl-amino, di-(lower alkyl)-amino-aryl-carbonyl-amino, lower alkyl-carbonyl-amino-aryl-carbonyl-amino, heterocyclyl-aryl-carbonyl-amino, lower cycloalkyl-carbonyl-amino, mono- or tetra-(lower

alkyl)-lower cycloalkyl-carbonyl-amino, heterocyclyl-carbonyl-amino, mono- or di-(lower alkyl)-heterocyclyl-carbonyl-amino, tri-(lower alkyl)-aryl-oxalyl-amino, lower alkyl-carbamoyl, or aryl-carbamoyl, thio, lower alkyl thio, lower cycloalkyl thio, aryl thio, heterocyclyl thio, lower alkyl sulphonyl, lower cycloalkyl sulphonyl, aryl sulphonyl, heterocyclyl sulphonyl.

Where there is more than one substituent, each substituent may be the same or different, for example tri-fluoromethyl, triphenylmethyl, 1-[1-methyl-1-[methylformyl]-2-phenyl] ethyl, or 2-[1-hydroxyl-3-cyclohexyl].

- 10 The term "unsubstituted lower alkyl" means an alkyl group as defined above where no substituents are present.

The term "lower alkenyl" means an alkenyl group containing from 2 to 7 carbon atoms, e.g. allyl, vinyl and butenyl.

- 15 The term "lower alkynyl" means an alkynyl group containing from 2 to 7 carbon atoms, e.g. propargyl or butynyl.

- The term "lower cycloalkyl", alone or in combination as in "lower cycloalkyl-lower alkyl", means a cycloalkyl group containing 3 to 10 carbon atoms, preferably 3 to 7 carbon atoms, e.g. cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and adamantyl, and which may be unsubstituted or substituted by e.g. one or more of lower alkyl, carboxyl, hydroxyl or aryl or optionally be benz-fused e.g. to aryl. Where there is more than one substituent, each substituent may be the same or different. Cyclopropylmethyl, 2-cyclobutyl-ethyl and 3-cyclohexyl-propyl are examples of lower cycloalkyl-lower alkyl groups.
- 20
- 25

The term "halo" denotes fluorine, chlorine, bromine or iodine.

- The term "lower alkoxy" denotes an unsubstituted or substituted lower alkyl group as defined hereinbefore, which is bonded via an oxygen atom, e.g. methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy, tert.-butoxy and the like. Suitable substituents are those applicable for "lower alkyl".
- 30

The term "aryl", alone or in combination as in "aryl-lower alkyl", means phenyl or naphthyl, optionally benz-fused, for example benz-fused to a lower cycloalkyl ring. "Aryl" denotes unsubstituted or substituted by e.g. one or more of halo, cyano, carboxyl,

- 5 lower alkyl-thio, nitro, oxo, hydroxyl, lower alkoxy, lower cycloalkyloxy, aryloxy, heterocyclyl oxy lower alkyl-heterocyclyl, heterocyclyl, lower alkoxy-carbonyl, lower alkyl-carbonyl, heterocyclyl-carbonyl, lower alkyl-heterocyclyl-carbonyl,
- 10 sulphamoyl, lower alkyl- sulphamoyl, thio, lower alkyl thio, lower cycloalkyl thio, aryl thio, heterocyclyl thio, lower alkyl-sulphonyl, lower cycloalkyl sulphonyl, aryl sulphonyl, heterocyclyl-sulphonyl, amino, mono- or di-(lower alkyl) amino, lower alkyl-sulphonyl-amino, di-(lower alkyl)-heterocyclyl-amino, lower alkyl-carbonyl-amino, (lower alkyl-carbonyl)(lower alkyl)-amino,
- 15 lower alkoxy-carbonyl-amino, aryl-carbonyl-amino, mono- or di-(lower alkyl)-carbamoyl, aryl-carbamoyl, lower alkyl, aryl-lower alkyl, amino-lower alkyl, heterocyclyl-lower alkyl, lower alkoxy-carbonyl-lower alkyl, lower alkyl- sulphamoyl-lower alkyl, aryl-sulphonyl-amino-lower alkyl, lower alkyl-sulphonyl-amino-lower alkyl, lower alkoxy-carbonyl-amino-lower alkyl,
- 20 heterocyclyl-oxy-carbonyl-amino-lower alkyl, aryloxy-carbonyl-amino-lower alkyl, lower alkyl-carbonyl-amino-lower alkyl, lower alkoxy-carbonyl-(lower alkyl)-amino-lower alkyl, lower alkyl-carbamoyl-lower alkyl, lower alkyl-aryl-carbonyl-amino-lower alkyl, aryl-carbamoyl-lower alkyl, lower cycloalkyl-carbonyl-amino-lower alkyl, heterocyclyl-carbonyl-amino-lower alkyl, or aryl-carbonyl-amino-lower alkyl. Where there is more than one
- 25 substituent, each substituent may be the same or different, for example 1-(3-methoxy-4-oxazolyl)phenyl, 1-(3-chloro-4-methoxy)phenyl, 1-(3-chloro-4-methyl) phenyl and 1-(3-fluoro-4-methyl)phenyl.

- The same substituents as listed above apply for all terms containing the phrase " phenyl" i.e.
- 30 substituted or unsubstituted) phenyl.

The term "aryloxy" denotes an aryl group as defined hereinbefore, which is bonded via an oxygen atom, e.g. phenoxy, and the like.

As used herein, the term "heterocyclyl", alone or in combination as in "heterocyclyl-lower alkyl", means a saturated, unsaturated or partially saturated monocyclic or bicyclic ring system which contains one or more hetero atoms selected from nitrogen, sulphur and oxygen; and
5 which is attached to the rest of the molecule via a carbon atom (C-linked), or a nitrogen atom (N-linked) in the ring system, and which is unsubstituted or substituted in the same manner as the aryl group defined hereinbefore and/or by oxido. Where there is more than one substituent, each substituent may be the same or different.

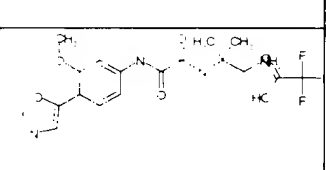
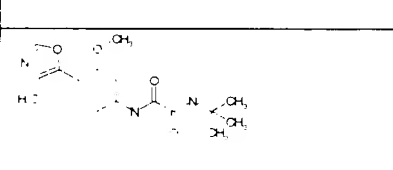
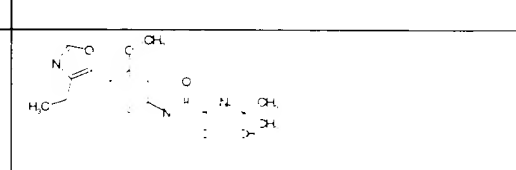
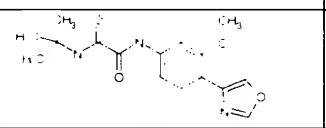
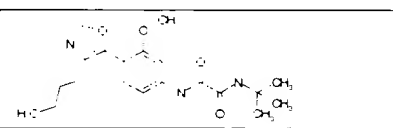
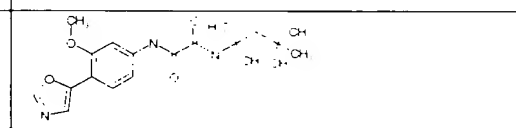
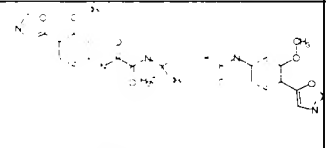
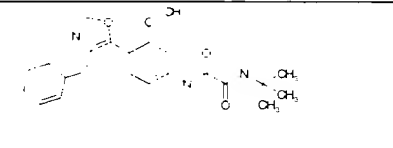
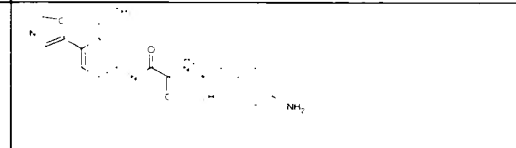
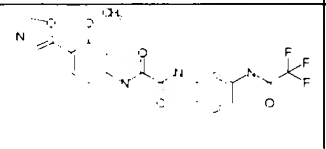
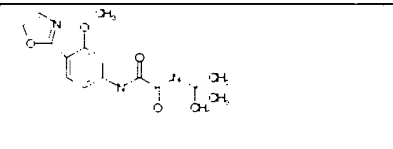
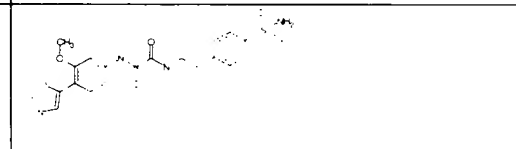
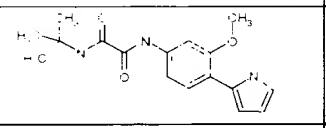
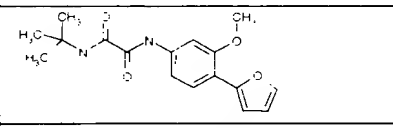
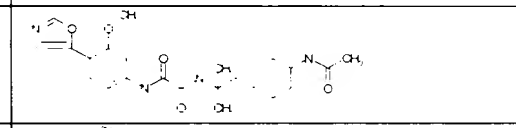
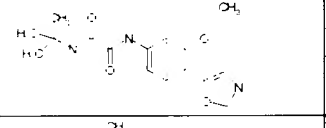
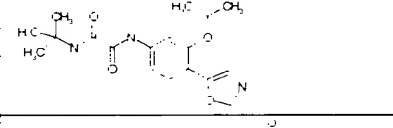
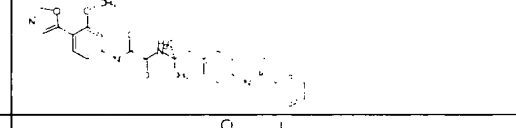
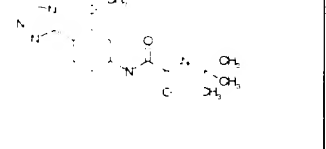
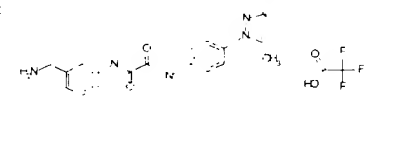
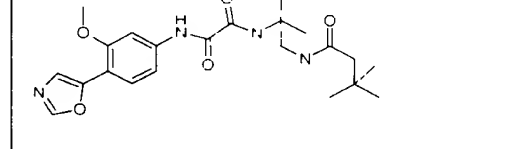
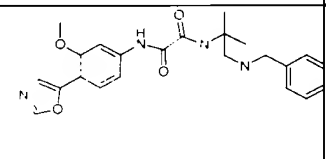
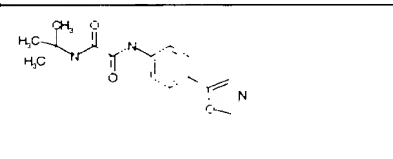
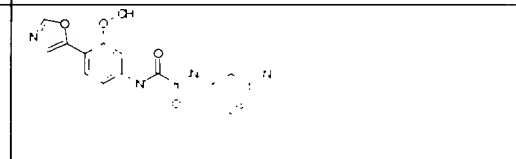
Examples of heterocyclyl groups are oxazolyl, isoxazolyl, furyl, tetrahydrofuryl, 1,3-dioxolanyl,
10 dihydropyranyl, thienyl, pyrazinyl, isothiazolyl, isoquinolyl, indolyl, indazolyl, quinolyl, dihydrooxazolyl, pyrimidinyl, benzofuranyl, tetrazolyl, pyrrolidinonyl, (N-oxide)-pyridinyl, pyrrolyl, triazolyl e.g. 1,2,4-triazolyl, pyrazolyl, benzotriazolyl, piperidinyl, morpholinyl, thiazolyl, pyridinyl, dihydrothiazolyl, imidazolidinyl, pyrazolinyl, benzothienyl, piperazinyl, imidazolyl, thiadiazolyl e.g. 1,2,3-thiadiazolyl, and benzothiazolyl.

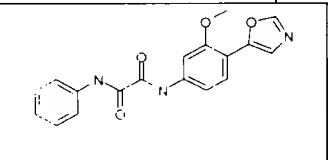
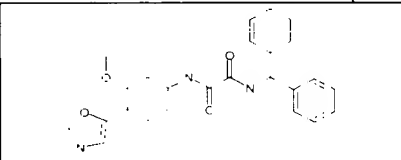
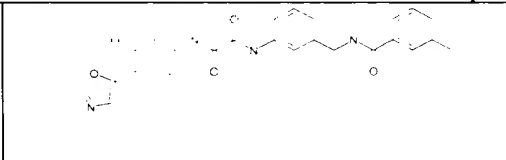
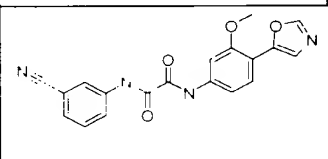
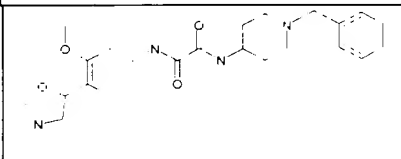
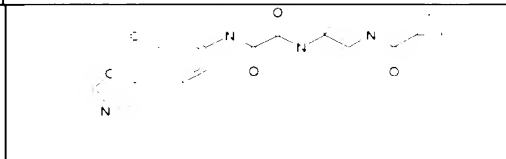
15 Any functional (i.e. reactive) group present in a side-chain may be protected, with the protecting group being a group which is known per se, for example, as described in "Protective Groups in Organic Synthesis", 2nd Ed., T.W. Greene and P.G.M. Wuts, John Wiley & Sons, New York, NY, 1991. For example, an amino group can be protected by a tert.-
20 butoxycarbonyl, formyl, trityl, benzyloxycarbonyl, 9-fluorenylmethyloxycarbonyl (Fmoc), trifluoroacetyl, 2-(biphenyl)isopropoxy-carbonyl or isobornyloxycarbonyl group or in the form of a phthalimido group; or a hydroxyl group can be protected by a tert.-butyldimethylsilyl, tetrahydropyranyl, 4-methoxybenzyl, or benzyl; or a carboxyl group can be protected in the form of an ester, for example as a methyl or tert.butyl ester. The protecting
25 group may be retained in the final compound or optionally removed by techniques known in the art.

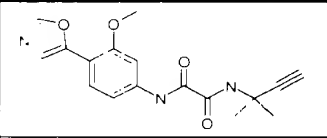
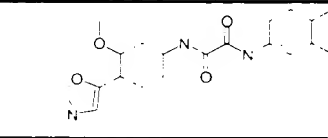
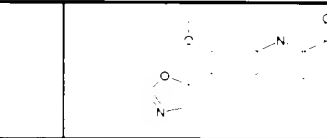
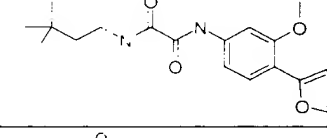
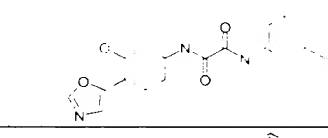
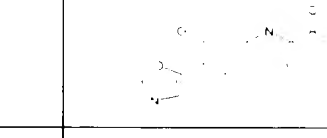
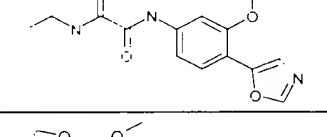
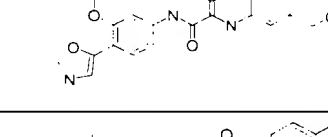
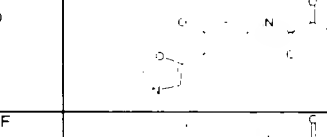
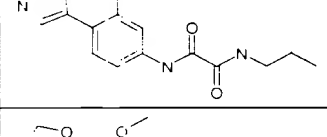
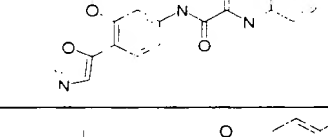
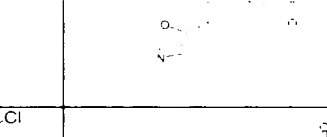
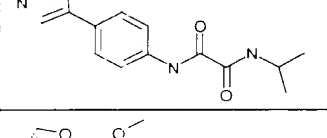
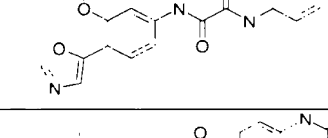
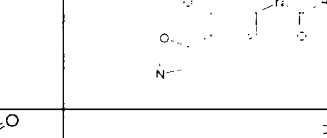
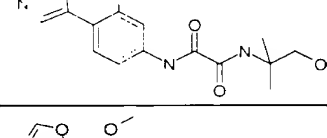
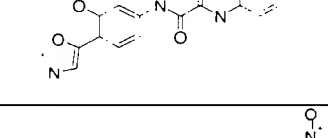

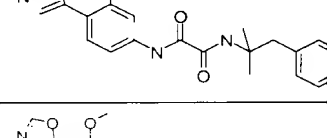
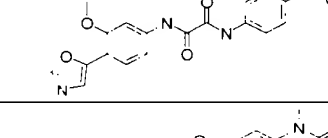
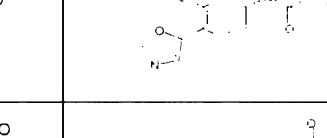
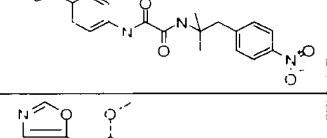
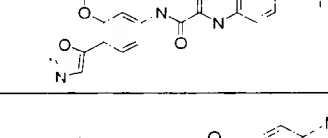

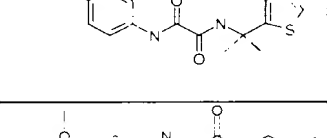
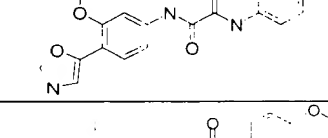
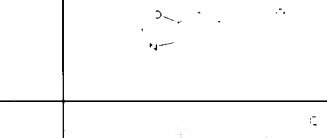
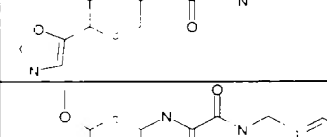
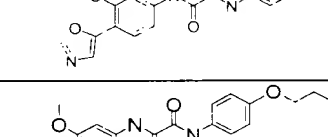
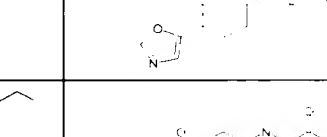
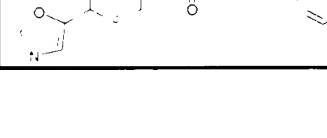
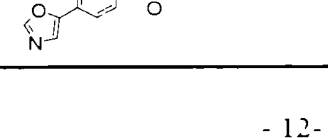

The compounds of this invention may contain one or more asymmetric carbon atoms and may therefore occur as racemates and racemic mixtures, single enantiomers, diastereomeric
30 mixtures and individual diastereomers. Furthermore, where a compound of the invention contains an olefinic double bond, this can have the (E) or (Z) configuration. Also, each chiral centre may be of the R or S configuration. All such isomeric forms of these compounds are embraced by the present invention.

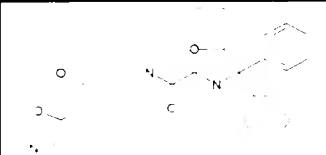
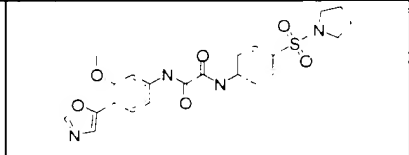
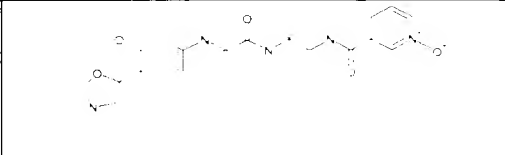
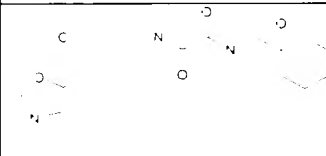
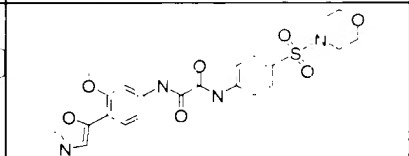
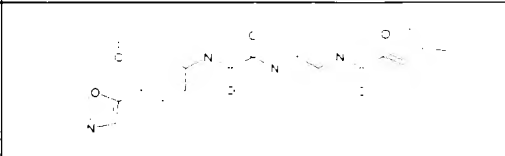
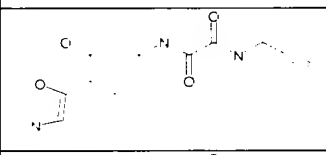
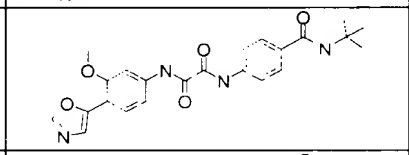
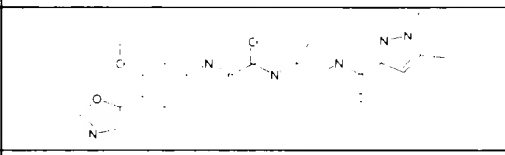
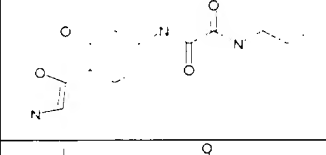
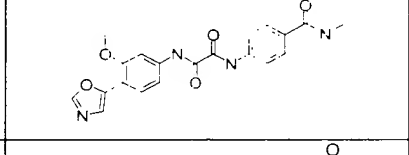
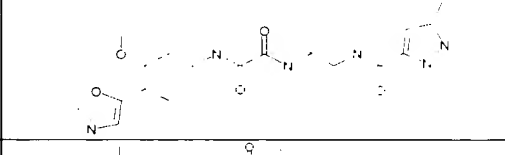
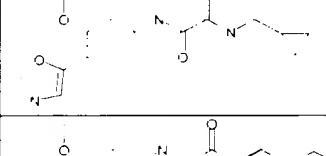
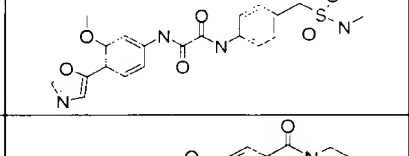
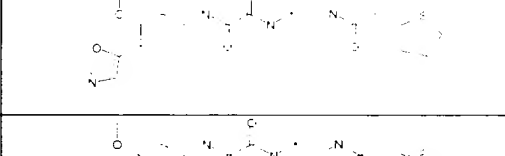
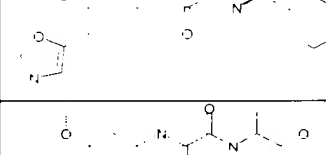
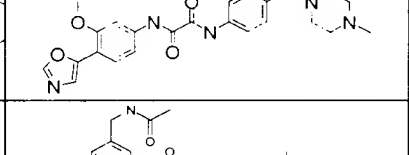
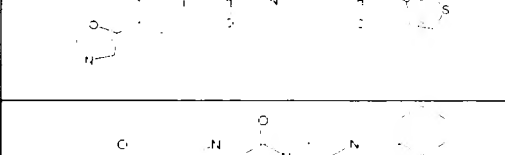
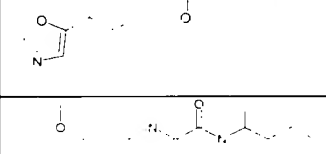
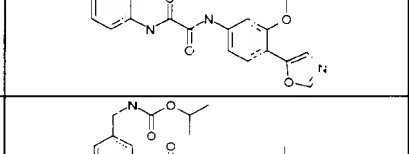
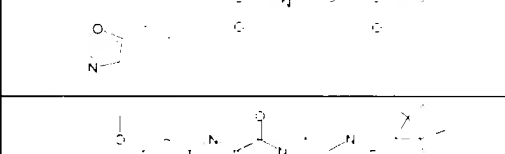
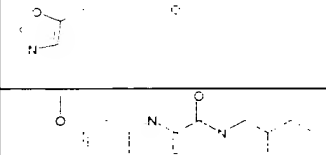
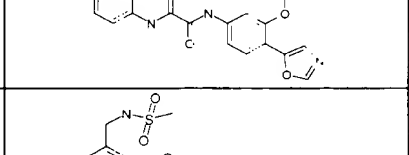
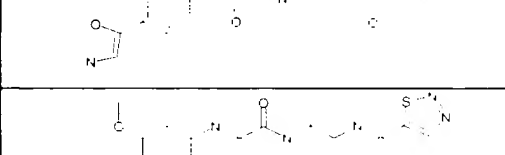
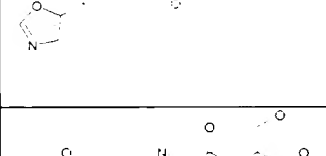
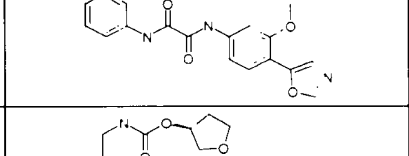
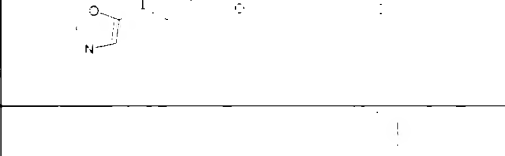
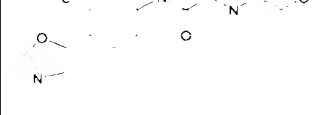
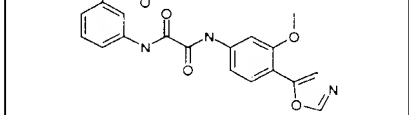
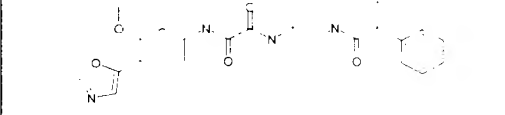
Examples of compounds of formula (I) are shown below in Table 1a and 1b:

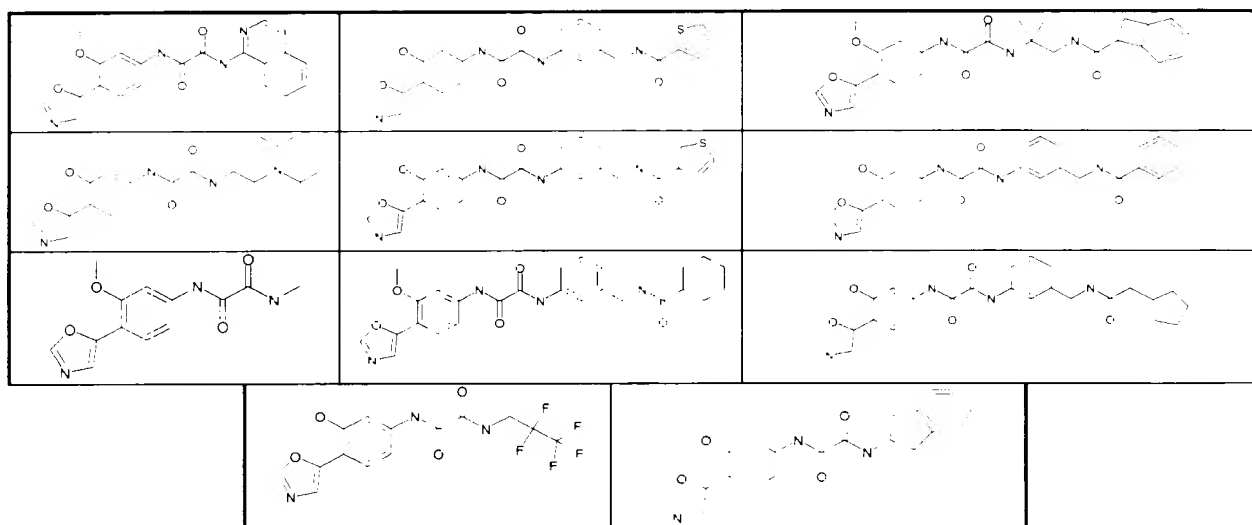
Table 1a

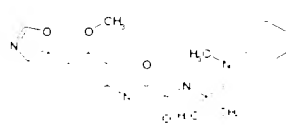
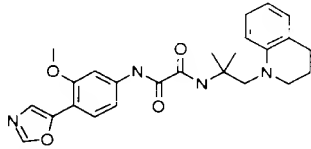
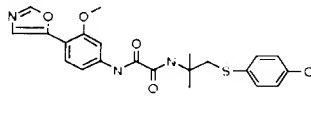
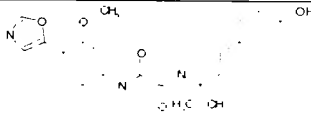
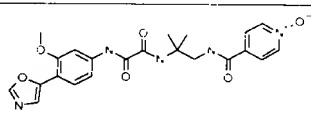
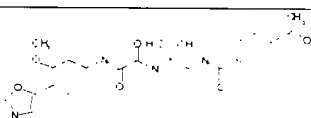
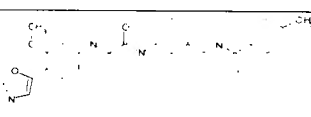
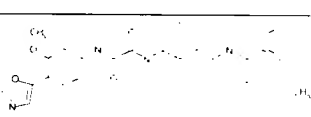
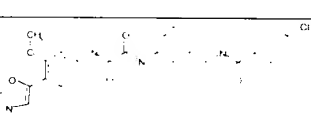
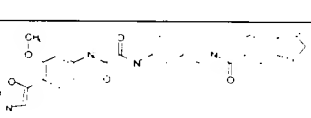
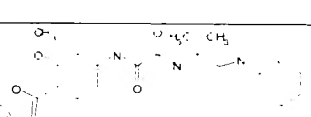
		
		
		
		
		
		
		
		
		
		

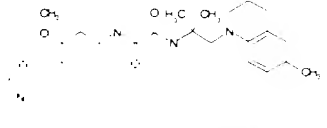
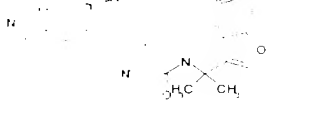
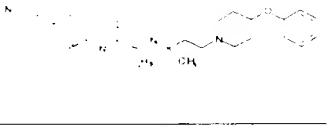
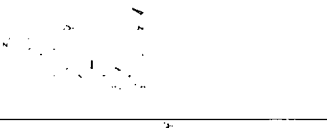

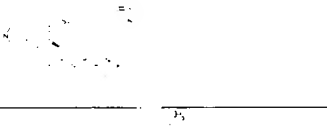
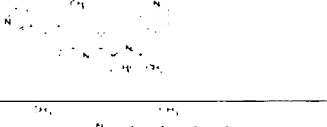
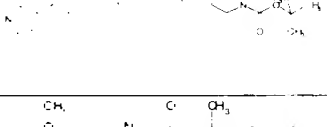



Compounds of formula (I), and formula (IX) below where R^2 is methoxy, R^4 , R^7 , and R^8 are as in formula (I) or formula (IX), and R^3 , R^5 , R^6 , R^9 , and R^{10} are hydrogen are shown in table 1b below.

table 1b

Name	Structure	MS(ES) (M+H) ⁺	Ex No
Benzyl 4-{2-[[[3-methoxy-4-(5-oxazolyl)phenylamino]oxalyl]amino]-2-methylpropyl}-1-piperidinecarboxylate		535	421
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(phenylthio)ethyl]oxalamide		426	422
N-[2-(1-Acetyl-4-piperidinyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		443	423
N-(2-Cyclohexyl-1,1-dimethylethyl)-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		400	424

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(N-methylanilino)ethyl]oxalamide		423	425
N-[2-(1,2,3,4-Tetrahydro-1-quinolyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		449	426
N-[2-(4-Hydroxyphenylthio)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		442	427
N-[3-(4-Hydroxyphenyl)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		424	598
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[(1-oxido-4-pyridyl)carboxamido]ethyl]oxalamide		454	599
N-[2-(4-Acetylbenzamido)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		479.1	600
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[3-[(4-methylbenzamido)methyl]phenyl]oxalamide		485.1	601
N-[3-[(2-Methoxybenzamido)methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		501.1	602
N-[3-[(4-Chlorobenzamido)methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		505.1	603
N-[3-[[[(1,3-Benzodioxol-5-yl)carboxamido]methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		515.2	604
N-[2-(2,3-Dihydro-1-indolyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		435	605

N-[2-(3,4-Dihydro-6-methyl-2H-quinol-1-yl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		463	606
N-[1-(3-Benzofuranyl)-1-methylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		420	607
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(4-phenoxy-piperidino)propyl]oxalamide		507	608
N-[2-(1-Butyryl-4-piperidiny)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		471	609
N-[2-[1-(Methanesulfonyl)-4-piperidiny]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		479	610
N-[2-[1-(Benzenesulfonyl)-4-piperidiny]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		541	611
N-[2-(1-Isobutyryl-4-piperidiny)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		471	612
tert-Butyl 4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino] oxalyl]amino]-3-methylbutyl]-1-piperidinecarboxylate		515	613
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(4-piperidiny)propyl]oxalamide		415	614

Preferred compounds of formula (I) and any of the compounds of formula (I) described below are those where at least one of R^2 , R^3 , R^5 and R^6 is not hydrogen especially where R^2 represents lower alkoxy, preferably methoxy.

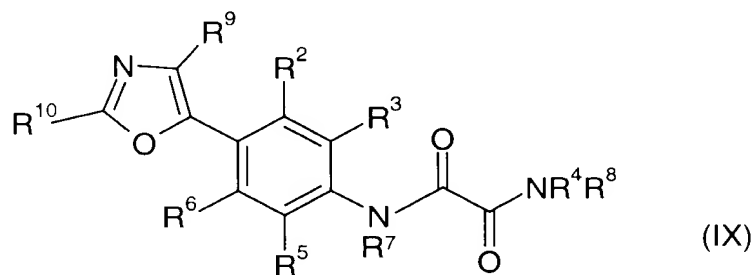
In preferred compounds of formula (I) and any of the compounds of formula (I) described below, R^1 represents a five-membered heterocycle with one to three heteroatoms selected from nitrogen, oxygen, and sulfur. Furthermore, preferred compounds of formula (I) are those where R^1 represents an unsubstituted or substituted oxazole ring or triazole ring. When substituted, the preferred substituents are methyl, ethyl, or benzyl.

Also preferred are compounds of formula (I) and any of the compounds of formula (I) described below as follows: where R^4 represents hydrogen or branched lower alkyl, and where R^3 , R^6 , and R^7 represent hydrogen. Most preferably, R^1 represents oxazolyl (especially unsubstituted), R^2 represents lower alkoxy (especially methoxy) and R^3 , R^4 , R^6 and R^7 represent hydrogen.

Also preferred are compounds of formula (I) and any of the compounds of formula (I) described below where R^8 represents branched lower alkyl, aryl, a 3 to 7 membered cycloalkyl ring, or a 5 or 6 membered monocyclic or 9 or 10 membered bicyclic saturated or unsaturated heterocyclic ring with 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulfur. These compounds may be substituted or unsubstituted as defined above. It is additionally preferred for these compounds that R^1 represents oxazolyl (especially unsubstituted), R^2 represents lower alkoxy (especially methoxy) and R^3 , R^4 , R^6 and R^7 represent hydrogen.

In formula (I) and any of the compounds of formula (I) described below, R^8 may be branched lower alkyl, aryl, and/or cycloalkyl, and/or a heterocyclic ring as defined immediately above.

In particular, preferred compounds of formula (I) are those of the general formula:



wherein

R^2 to R^8 are defined as above; and,

R⁹ is hydrogen, lower alkyl, aryl-lower alkyl;

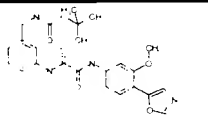
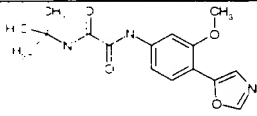
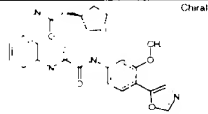

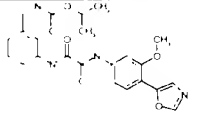
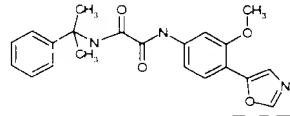
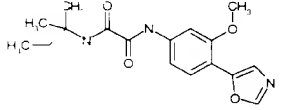
R¹⁰ is hydrogen.

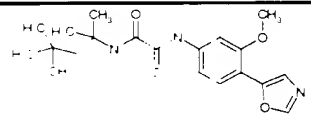
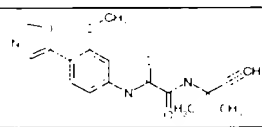
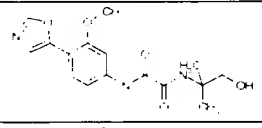
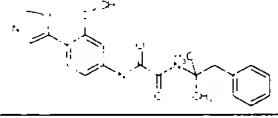
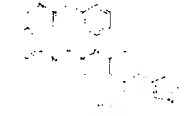
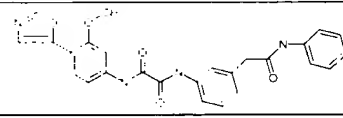
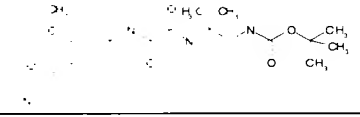
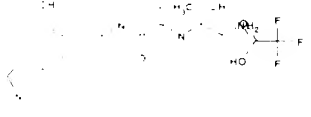
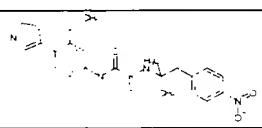
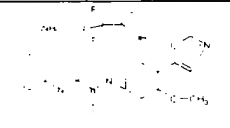

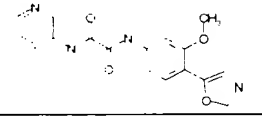

In some compounds of formula (IX), R⁹ represents methyl, ethyl, or benzyl, and R¹⁰ preferably
 5 is hydrogen. In others, R⁹ and R¹⁰ both represent hydrogen. It is preferred that R⁸ represents
 branched lower alkyl, aryl, a 3 to 7 membered cycloalkyl ring, or a 5 or 6 membered
 monocyclic or 9 or 10 membered bicyclic saturated or unsaturated heterocyclic ring with 1 to 4
 heteroatoms selected from nitrogen, oxygen, and sulfur, and in addition is preferred that R²
 represent lower alkoxy, R³, R⁴, R⁶, and R⁷ represent hydrogen.

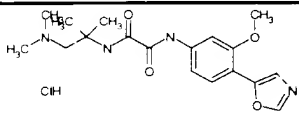
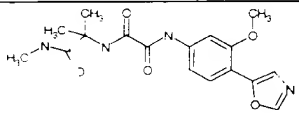
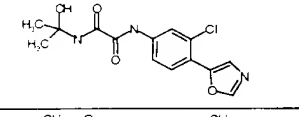
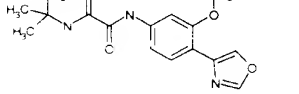
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More particularly, preferred compounds of formula (I) are those of the general formula (IX),
 wherein R² is methoxy or chloro; R³, R⁴, R⁵, R⁶, R⁷, R⁹, and R¹⁰ are hydrogen, and
 R⁸ is heterocyclyl, aryl, or branched chain lower alkyl;

15 Examples of such compounds are:

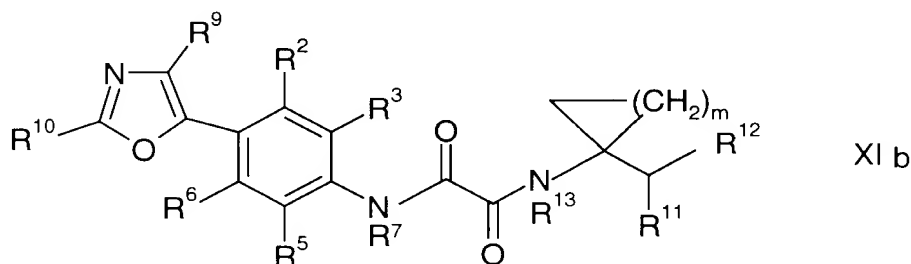
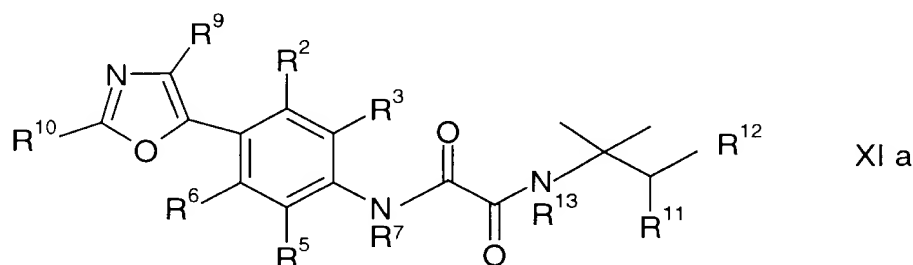
	tert-Butyl[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]benzyl]carbamate
	N-tert-Butyl-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide
	[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]benzyl]carbamic acid tetrahydro-3(S)-furyl ester
	N-[3-(Benzamidomethyl)phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide
	Isopropyl [3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]benzyl]carbamate
	N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-(1-methyl-1-phenylethyl)oxalamide
	N-(1,1-Dimethylpropyl)-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide

	N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-(1,1,3,3-tetramethyl-butyl)oxalamide
	N-(1,1-Dimethylpropargyl)-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide
	N-(2-Hydroxy-1,1-dimethylethyl)-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide
	N-(1,1-Dimethyl-2-phenylethyl)-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide
	Phenyl [3-[[[4-(5-oxazolyl)anilino]oxalyl]amino]benzyl]carbamate
	N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[3-[(phenylcarbamoyl)methyl]phenyl]oxalamide
	tert-Butyl [2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]carbamate
	N-(2-Amino-1,1-dimethylethyl)-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide trifluoroacetate (1:1)
	N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(4-nitrophenyl)ethyl]oxalamide
	N-[3-(Aminomethyl)phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide trifluoroacetate (1:1)
	Methyl [3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]benzyl]carbamate
	N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-(3-pyridyl)oxalamide
	N-[3-[(Benzenesulfonamido)methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide

	N-(2-Dimethylamino-1,1-dimethylethyl)-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide hydrochloride (1:1)
	N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1-methyl-1-(methylcarbamoyl)ethyl]oxalamide
	N-tert-Butyl-N'-[3-chloro-4-(5-oxazolyl)phenyl]oxalamide
	N-tert-Butyl-N'-[3-methoxy-4-(4-oxazolyl)phenyl]oxalamide

or their pharmaceutically acceptable salts.

In particular, preferred compounds of formula (I) and (IX) are also those of the general formulas:



5

wherein R^2 , R^3 , R^5 , R^6 , R^7 , R^9 and R^{10} are defined as above

R^{11} and R^{13} is H or lower alkyl, $m=1$ to 5 and

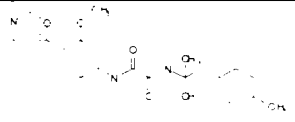
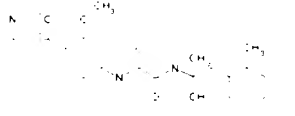
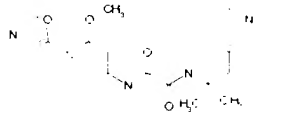
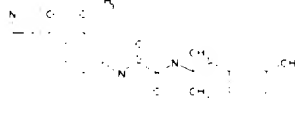
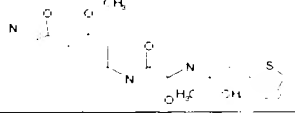
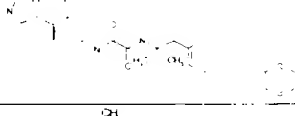
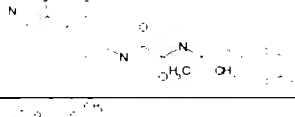
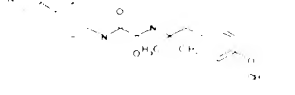
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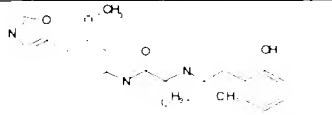
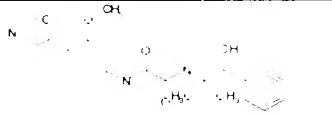
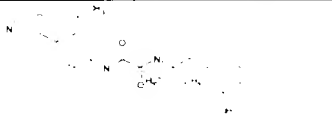
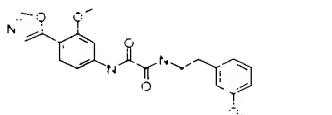
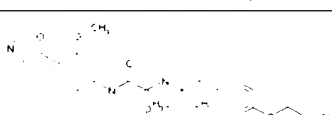
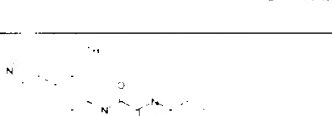
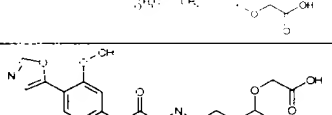
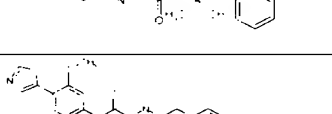
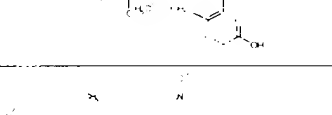
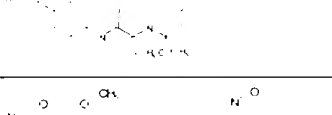
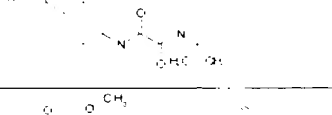
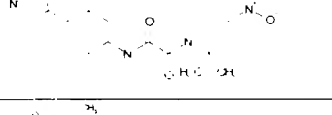
R^{12} is heterocyclyl, or aryl (substituted or unsubstituted) other than 4-fluorophenyl.

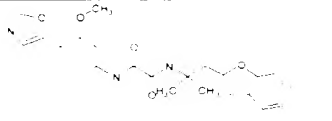
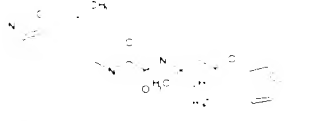
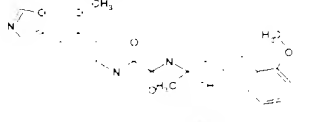
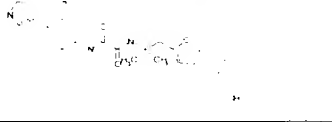
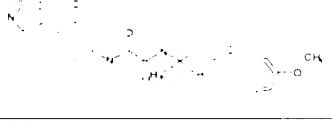

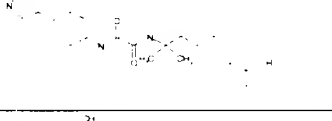
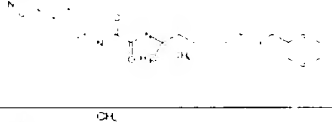
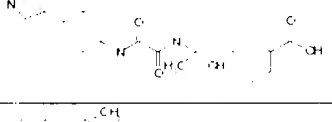
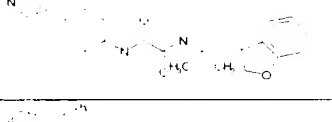
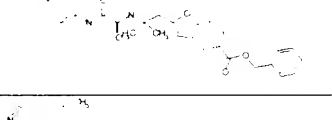
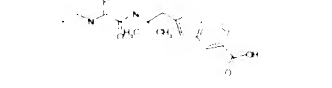
Particularly preferred compounds of formula (XIa or XIb) are those wherein

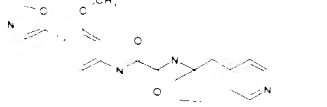
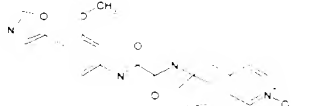
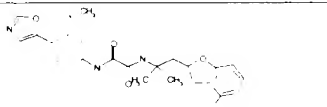
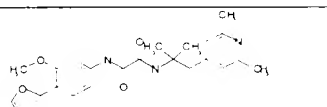
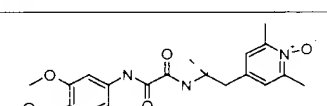
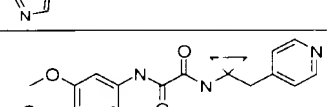
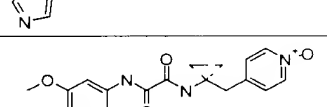
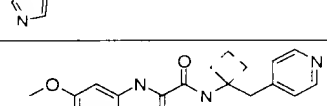
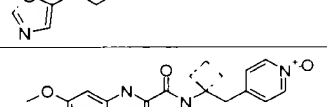
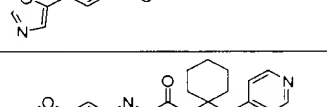
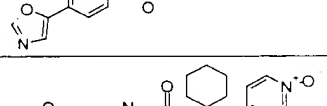
- 5 R^2 is methoxy, R^3 , R^5 , R^6 , R^9 , R^{10} , R^{11} and R^{13} are hydrogen and wherein R^{12} is (unsubstituted or substituted) phenyl other than 4-fluorophenyl and (unsubstituted or substituted heteroaryl). Also preferred are those compounds where R^{12} represents a 5 or 6 membered monocyclic or a 9 or 10 membered bicyclic saturated or unsaturated heteroaromatic ring with 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulfur.

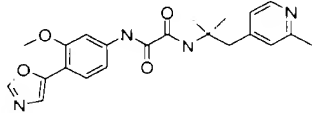
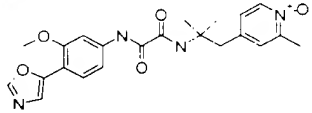
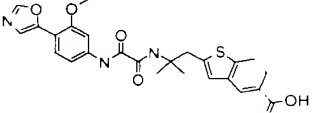
- 10 Examples of such compounds are listed in table 1c

table 1c			
Name	Structure	MS(ES) (M+H) ⁺	Ex No
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(4-methylphenyl)ethyl]oxalamide		408	302
N-[1,1-Dimethyl-2-(2-methylphenyl)ethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		408	303
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(3-pyridyl)ethyl]oxalamide		395	304
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(3-methylphenyl)ethyl]oxalamide		408	305
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(2-thienyl)ethyl]oxalamide		400	306
N-[2-(4-Benzoyloxy-phenyl)-1,1-dimethyl-ethyl]-N'-(3-methoxy-4-oxazol-5-yl-phenyl)-oxalamide		500	307
N-[2-(4-Hydroxy-phenyl)-1,1-dimethyl-ethyl]-N'-(3-methoxy-4-oxazol-5-yl-phenyl)-oxalamide		410	308
N-(3-Methoxy-4-oxazol-5-yl-phenyl)-N'-[2-(4-methoxy-phenyl)-1,1-dimethyl-ethyl]-oxalamide		424	309

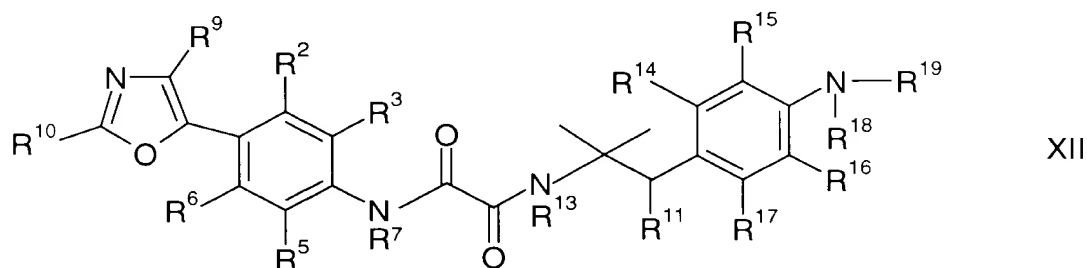
N-[2-(2-Hydroxy-phenyl)-1,1-dimethyl-ethyl]-N'-(3-methoxy-4-oxazol-5-yl-phenyl)-oxalamide		410	310
N-(1,1-Dimethyl-2-phenyl-propyl)-N'-(3-methoxy-4-oxazol-5-yl-phenyl)-oxalamide		408	311
N-[2-(3-Hydroxy-phenyl)-1,1-dimethyl-ethyl]-N'-(3-methoxy-4-oxazol-5-yl-phenyl)-oxalamide		410	312
N-(3-Methoxy-4-oxazol-5-yl-phenyl)-N'-[2-(3-methoxy-phenyl)-1,1-dimethyl-ethyl]-oxalamide		424	313
N-[2-[4-(Cyanomethoxy)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		449	314
2-[4-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]phenoxy]acetic acid		468	315
2-[2-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]phenoxy]acetic acid		468	438
2-[3-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]phenoxy]acetic acid		468	439
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(1-oxido-4-pyridyl)ethyl]oxalamide		411	440
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(1-oxido-3-pyridyl)ethyl]oxalamide		411	441
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(1-oxido-2-pyridyl)ethyl]oxalamide		411	442
2-[3-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]phenoxy]acetic acid		468	443

N-[2-(2-Benzofuranyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		434	444
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(3-methyl-2-benzofuranyl)ethyl]oxalamide		448	445
N-[2-(7-Methoxy-2-benzofuranyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		464	446
N-[2-(5-Methoxy-2-benzofuranyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		464	447
N-[2-(6-Methoxy-2-benzofuranyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		464	448
Benzyl 4-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]benzoate		528	449
4-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]benzoic acid		438	450
Benzyl 3-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]benzoate		528	451
3-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]benzoic acid		438	452
N-[2-(3-Benzofuranyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		434	453
Benzyl 2-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]-5-benzofurancarboxylate		568	454
2-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]-5-benzofurancarboxylic acid		477.9	455

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1-[(4-pyridyl)methyl]-1-cyclopentyl]oxalamide		421	456
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1-[(1-oxido-4-pyridyl)methyl]-1-cyclopentyl]oxalamide		437	457
N-[2-(4-Methoxy-2-benzofuranyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		464	458
N'-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-(2,6-dimethyl-4-pyridyl)-1,1-dimethylethyl]oxalamide		423.22	653
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(2,6-dimethyl-1-oxido-4-pyridyl)ethyl]oxalamide		439.3	654
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1-[(4-pyridyl)methyl]-1-cyclopropyl]oxalamide		393	655
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1-[(1-oxido-4-pyridyl)methyl]-1-cyclopropyl]oxalamide		409	656
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1-[(4-pyridyl)methyl]-1-cyclobutyl]oxalamide		407	657
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1-[(1-oxido-4-pyridyl)methyl]-1-cyclobutyl]oxalamide		421	658
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1-[(4-pyridyl)methyl]-1-cyclohexyl]oxalamide		435	659
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1-[(1-oxido-4-pyridyl)methyl]-1-cyclohexyl]oxalamide		451	660

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(2-methyl-4-pyridyl)ethyl]oxalamide		409	661
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(2-methyl-1-oxido-4-pyridyl)ethyl]oxalamide		425	662
2-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]-5-benzothiophenecarboxylic acid		494	663

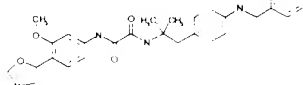
Particularly preferred compounds of formula (I) and (IX) are also those of the general formula

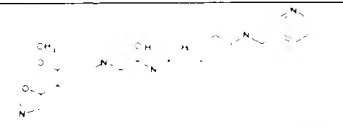
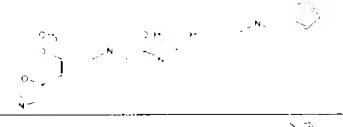
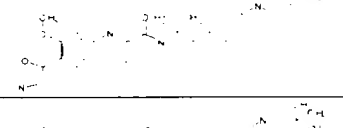
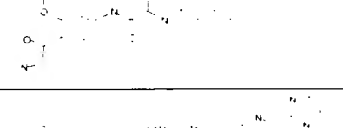
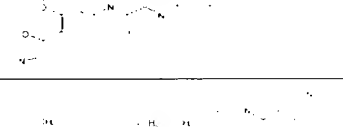
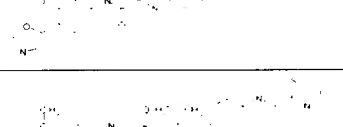
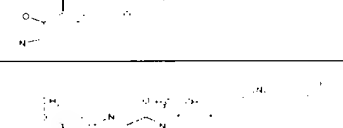
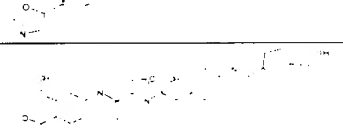
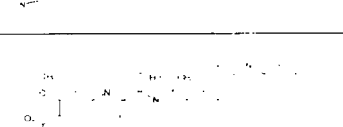
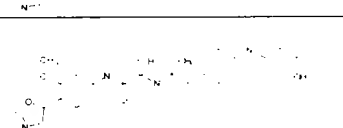
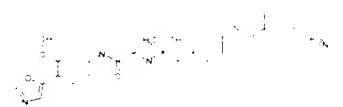



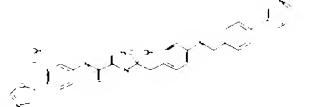
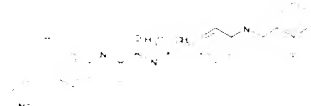
- 5 wherein $R^2, R^3, R^5, R^6, R^7, R^9$ and R^{10} are defined as above, $R^{11}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17}$ and R^{18} are H or lower alkyl and R^{19} is alkyl, cycloalkylalkyl, heterocycl alkyl or aryl alkyl.

- Particularly preferred compounds of formula (XII) are those wherein R^2 is methoxy and $R^3, R^5, R^6, R^9, R^{10}, R^{11}$ and R^{13} are hydrogen. Also preferred are compounds wherein R^{19} represents
10 arylalkyl, branched lower alkyl, a 3 to 7 membered cycloalkyl alkyl, or a 5 or 6 membered monocyclic or 9 or 10 membered bicyclic saturated or unsaturated heterocycl alkyl with 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulfur.

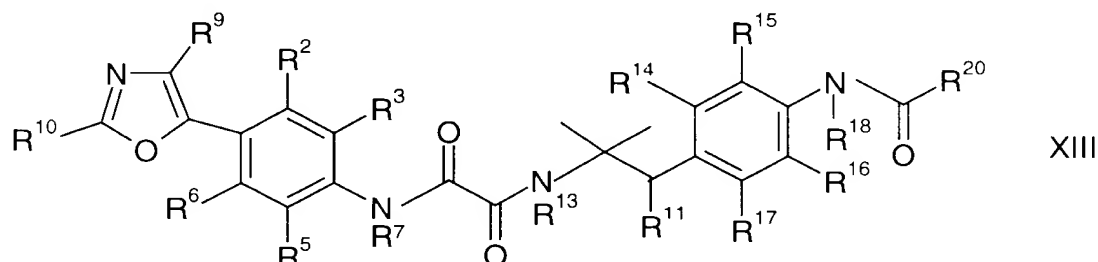
Examples of such compounds are listed in table 1d below

Name	Structure	MS(ES) (M+H) ⁺	Ex No
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(2-pyridinyl)methylamino]phenyl]ethyl]oxalamide		500.1	316

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(3-pyridyl)methylamino]phenyl]ethyl]oxalamide		500.1	317
N-[2-[4-(2-Furfurylamino)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		489.1	318
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-Dimethyl-2-[4-(2-thenylamino)phenyl]ethyl]oxalamide		505.1	319
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2,2-dimethylpropylamino)phenyl]ethyl]oxalamide		479.2	320
N-[2-[4-[(1H-Imidazol-2-yl)methylamino]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		489.1	321
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(4-pyridyl)methylamino]phenyl]ethyl]oxalamide		500.1	322
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(2-thiazolyl)methylamino]phenyl]ethyl]oxalamide		506.1	323
N-[2-[4-(3-Furfurylamino)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		489.1	324
N-[2-[4-[5-(Hydroxymethyl)-2-furfurylamino]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		519.1	325
N-[2-(4-Benzylaminophenyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		499.1	326
N-[2-[4-(2-Hydroxybenzylamino)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		515.1	327
N-[2-[4-(3-Cyanobenzylamino)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		524.1	328

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[4-(3-pyridyl)benzylamino]phenyl]ethyl]oxalamide		576.2	329
N-[2-[4-(2-Fluorobenzylamino)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		517.1	330

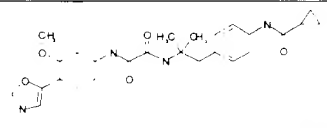
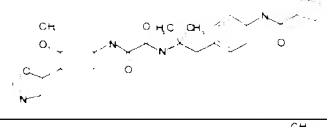
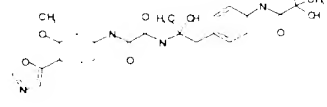
Particularly preferred compounds of formula (I) and (IX) are also those of general formula

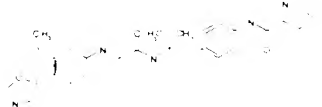

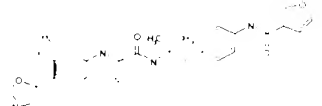
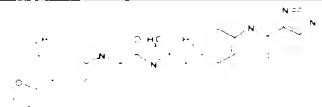
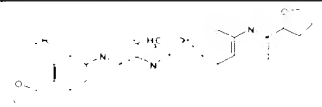
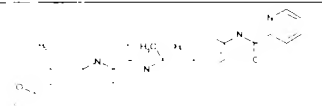
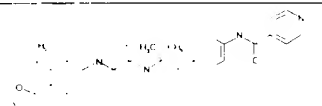
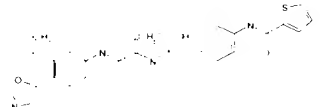
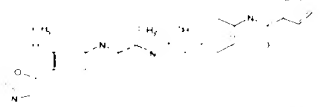
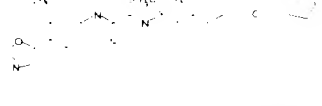
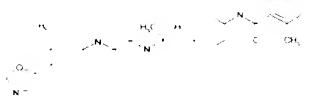
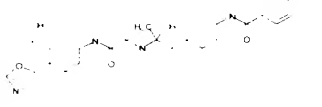


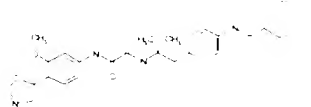

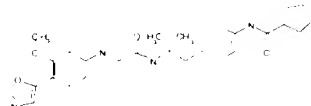
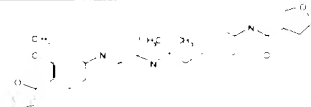
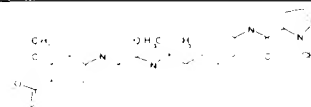
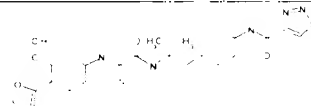
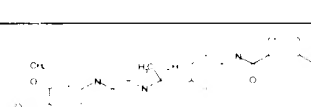
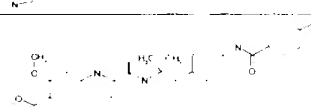
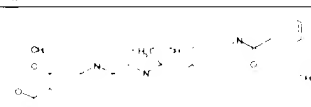
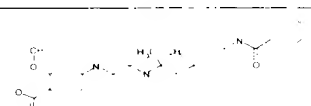
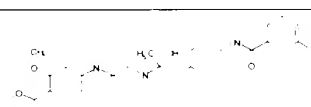
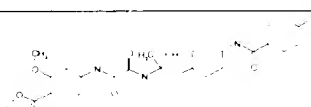
wherein $R^2, R^3, R^5, R^6, R^7, R^9$ and R^{10} are defined as above, $R^{11}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17}$ and R^{18} are H or lower alkyl and R^{20} is alkyl, cycloalkyl, aryl, heterocyclyl.

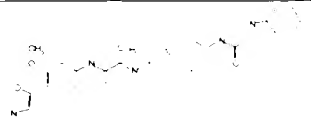
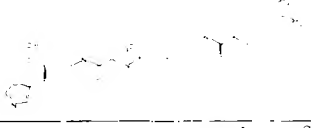

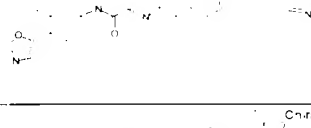
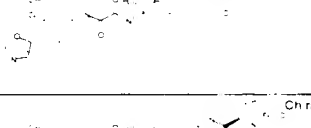
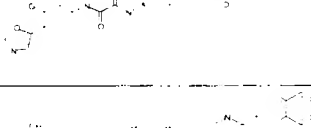
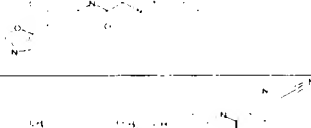
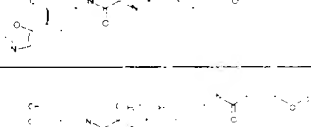
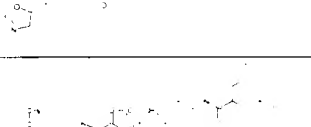
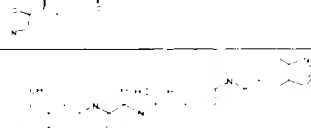
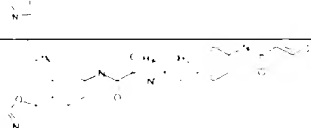
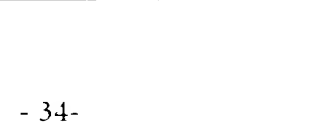
Particularly preferred compounds of formula (XIII) are those wherein R^2 is methoxy and $R^3, R^5, R^6, R^9, R^{10}, R^{11}$ and R^{13} are hydrogen. Also preferred are compounds where R^{20} represents aryl, branched lower alkyl, a 3 to 7 membered cycloalkyl ring, or a 5 or 6 membered or 9 or 10 membered bicyclic saturated or unsaturated heterocyclic ring with 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulfur.

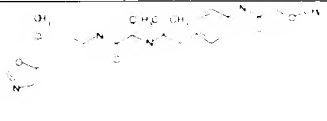
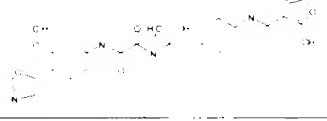
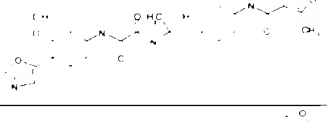


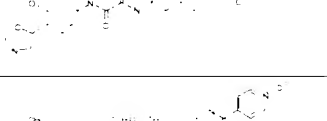
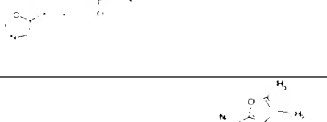
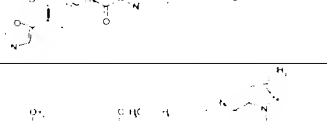
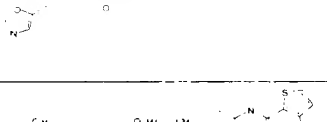
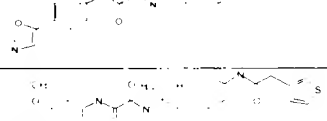

Examples of such compounds are listed in table 1e below



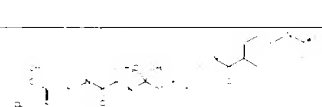
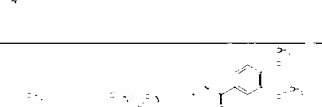
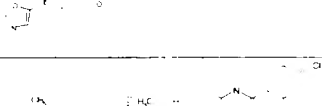
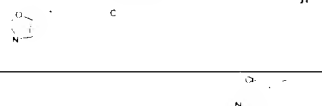
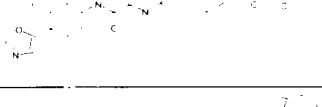
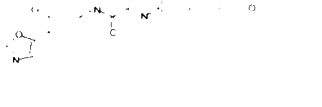
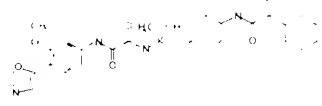
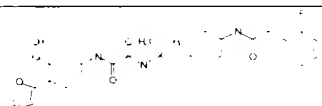
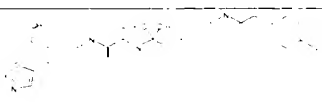
Table 1e			
Name	Structure	MS(ES) (M+H) ⁺	Ex No
N-[2-[4-(Cyclopropylcarboxamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		477.1	331
N-[2-[4-(Cyclobutylcarboxamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		491.1	332
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(4-pivalamidophenyl)-1,1-dimethylethyl]oxalamide		493.1	333

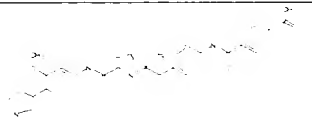
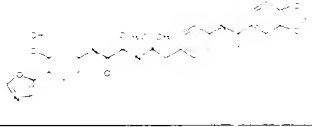
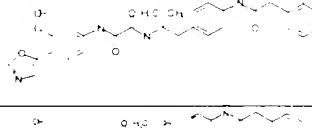

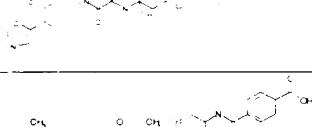
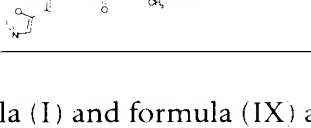
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(1H-pyrrol-2-yl)carboxamido]phenyl]ethyl]oxalamide		502.1	334
N-[2-[4-[(2-Furyl)carboxamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		503.1	335
N-[2-[4-[(3-Furyl)carboxamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		503.1	336
N-[2-[4-[(1H-Imidazol-4-yl)carboxamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		503.1	337
N-[2-[4-[(Tetrahydro-2(RS)-furyl)carboxamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		507.2	338
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(2-pyridyl)carboxamido]phenyl]ethyl]oxalamide		514.1	339
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(4-pyridyl)carboxamido]phenyl]ethyl]oxalamide		514.1	340
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(2-thienyl)carboxamido]phenyl]ethyl]oxalamide		519.1	341
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N-[1,1-dimethyl-2-[4-[(3-thienyl)carboxamido]phenyl]ethyl]oxalamide		519.1	342
N-[2-[4-(2-Cyclopentylacetamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		519.2	343
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-methylbenzamido)phenyl]ethyl]oxalamide		527.2	344
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(4-methylbenzamido)phenyl]ethyl]oxalamide		527.2	345

N-[2-[4-(Cycloheptylcarboxamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		533.2	346
N-[2-[4-(5-Isoxazolyl)carboxamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		504.1	347
N-[2-[4-(Cyclopentylcarboxamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		505.2	348
N-[2-[4-[(Tetrahydro-3(RS)-furyl)carboxamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		507.1	349
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(1-methyl-1H-pyrrol-2-yl)carboxamido]phenyl]ethyl]oxalamide		516.1	350
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-(1,1-dimethyl-2-[4-[(1,2,3-thiadiazol-4-yl)carboxamido]phenyl]ethyl]oxalamide		521.1	351
N-[2-[4-(3-Fluorobenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		531.1	352
N-[2-[4-(4-Fluorobenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		531.1	353
N-[2-[4-(2-Methoxybenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		543.2	354
N-[2-[4-(2-Chlorobenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		547.1	355
N-[2-[4-(3-Chlorobenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		547.1	356
N-[2-[4-(4-Chlorobenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		547.1	357

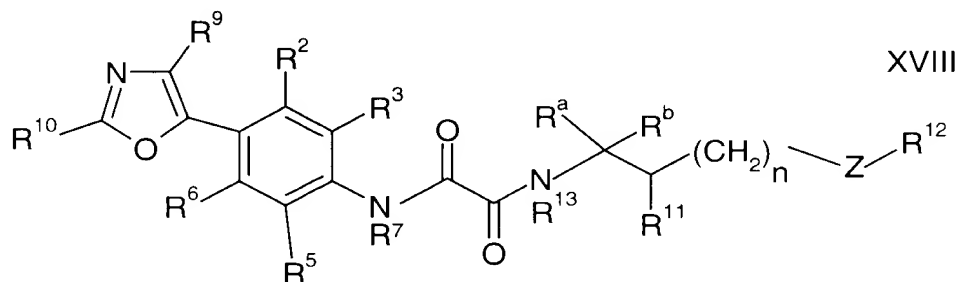
N-[2-[4-[(1H-Indol-2-yl)carboxamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		552.1	358
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[4-(dimethylamino)benzamido]phenyl]ethyl]oxalamide		556.1	359
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(3,3-dimethylbutyramido)]phenyl]ethyl]oxalamide		507.1	360
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[2-(1-tetrazolyl)acetamido]phenyl]ethyl]oxalamide		519.1	361
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(5-oxo-2(S)-pyrrolidinyl)carboxamido]phenyl]ethyl]oxalamide		520.1	362
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(5-oxo-2(R)-pyrrolidinyl)carboxamido]phenyl]ethyl]oxalamide		520.1	363
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(2-naphthyl)carboxamido]phenyl]ethyl]oxalamide		563.1	364
N-[2-[4-[(6-Cyano-3-pyridyl)carboxamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		580.1 (M+H+ ACN)	365
N-[2-[4-(3-Methoxybenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		543.1	366
N-[2-[4-(3,5-Difluorobenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		549.1	367
N-[2-[4-[(1H-Indol-5-yl)carboxamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		552.1	368
(E)-N-[2-[4-(2-Butenamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		477.1	369

N-[2-[4-(2-Methoxyacetamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		481.2	370
N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(2-methyl-3-furyl)carboxamido]phenyl]ethyl]oxalamide		517.1	371
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(5-methyl-4-isoxazolyl)carboxamido]phenyl]ethyl]oxalamide		518.1	372
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(3-methyl-4-isoxazolyl)carboxamido]phenyl]ethyl]oxalamide		518.1	373
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(5-methyl-3-isoxazolyl)carboxamido]phenyl]ethyl]oxalamide		518.1	374
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(1-oxido-3-pyridyl)carboxamido]phenyl]ethyl]oxalamide		530.1	375
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(1-oxido-4-pyridyl)carboxamido]phenyl]ethyl]oxalamide		530.1	376
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(4,5-dimethyl-2-furyl)carboxamido]phenyl]ethyl]oxalamide		531.1	377
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(2,5-dimethyl-2H-pyrazol-3-yl)carboxamido]phenyl]-1,1-dimethylethyl]oxalamide		531.1	378
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(3-methyl-2-thienyl)carboxamido]phenyl]ethyl]oxalamide		533.1	379
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[2-(3-thienyl)acetamido]phenyl]ethyl]oxalamide		533.1	380

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(4-methyl-2-thienyl)carboxamido]phenyl]ethyl]oxalamide		533.1	381
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(4-methyl-1,2,3-thiadiazol-5-yl)carboxamido]phenyl]ethyl]oxalamide		535	382
N-[2-[4-(4-Acetamidobenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		570.1	383
N-[2-[4-(3,4-Dimethoxybenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		573.1	384
N-[2-[4-(4-Chloro-2-methoxybenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		578.2	385
N-[2-[4-(2,6-Dichlorobenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		581	386
N-[2-[4-[(Bicyclo[4.2.0]octa-1(6),2,4-triene-7(RS)-yl)carboxamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		539.1	387
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-oxo-2-phenylacetamido)phenyl]ethyl]oxalamide		541.1	388
N-[2-[4-[2-(2-Fluorophenyl)acetamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		545	389
N-[2-[4-[2-(4-Fluorophenyl)acetamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		545	390
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N-[2-[4-[(4-methoxy-3-thienyl)carboxamido]phenyl]-1,1-dimethylethyl]oxalamide		549	391

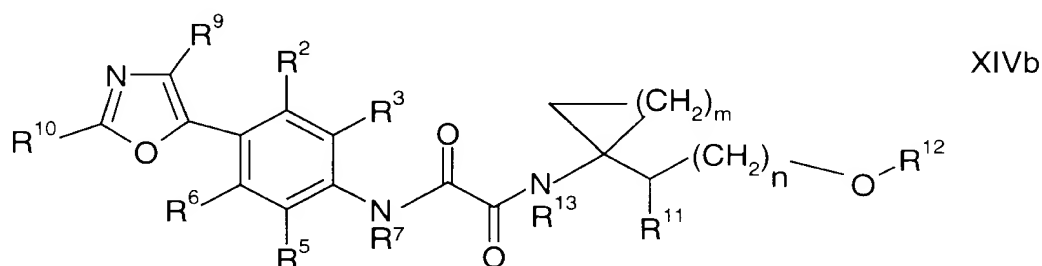
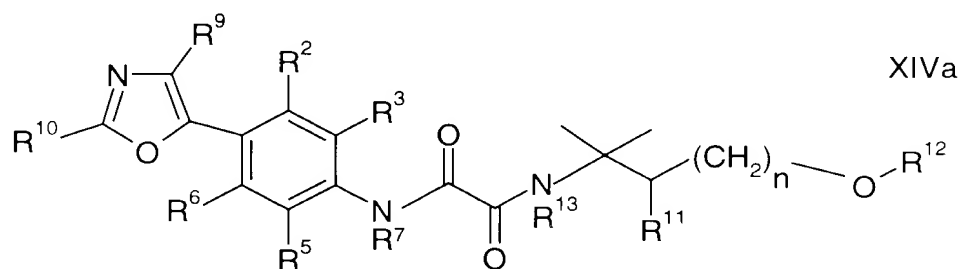
N-[2-[4-(4-Acetylbenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		555.1	392
N-[2-[4-[(1,3-Benzodioxol-5-yl)carboxamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		557.1	393
N-[2-[4-[2-(2-Chlorophenyl)acetamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		561.1	394
N-[2-[4-[2-(4-Chlorophenyl)acetamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		561.1	395
tert-Butyl 4-[[4-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]phenyl]carbamoyl]benzoate		613	596
4-[[[4-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]phenyl]carbamoyl]benzoic acid		557	597

Particularly preferred compounds of formula (I) and formula (IX) are also those of general formula



wherein R^2 , R^3 , R^5 , R^6 , R^7 , R^9 and R^{10} are defined as above, R^{11} and R^{13} are H or lower alkyl, $n=0$ or 1 , R^a , R^b are lower alkyl or R^a and R^b taken together with the carbon atom to which they are attached form a 3 to 7 member carbocycle, and R^{12} is heterocyclyl, aryl or lower cycloalkyl and Z is O, S or NR^{28} , wherein R^{28} is H or lower alkyl.

Further preferred compounds of formula XVIII are those of general formulas:



wherein R^2 , R^3 , R^5 , R^6 , R^7 , R^9 and R^{10} are defined as above; R^{11} and R^{13} is H or lower alkyl, $n = 0$ or 1, $m = 1$ to 5 and, R^{12} is heterocyclyl, aryl or lower cycloalkyl.

5

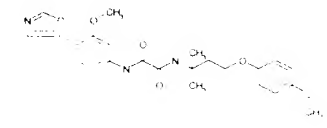
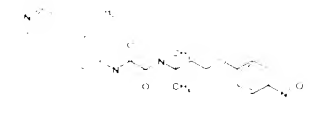
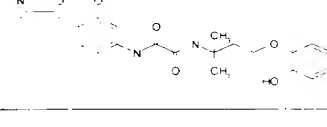
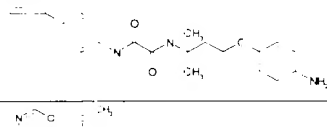
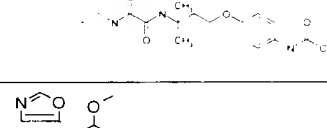
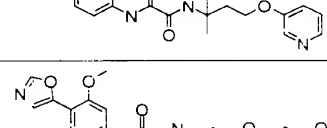
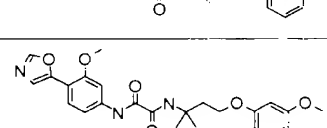
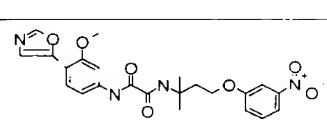
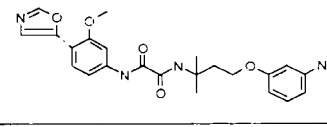
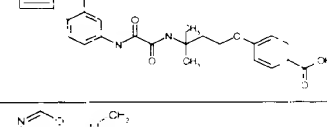
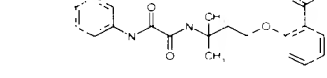

Particularly preferred compounds of formulae (XVIII), and (XIVa and XIVb) are those wherein R^2 is methoxy and R^3 , R^5 , R^6 , R^9 , R^{10} , R^{11} and R^{13} are hydrogen.

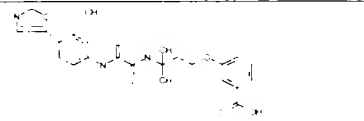
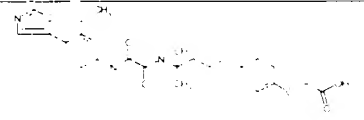
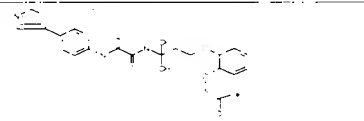
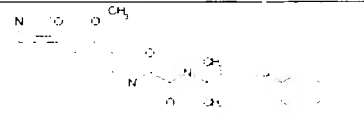

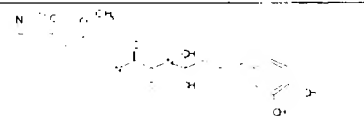
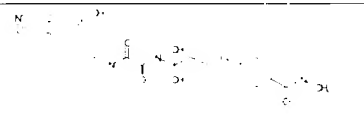
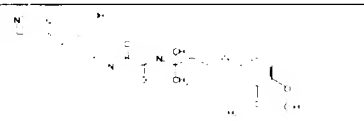
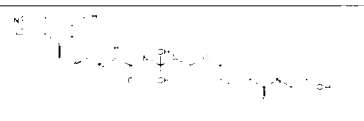
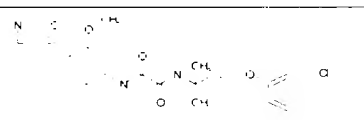
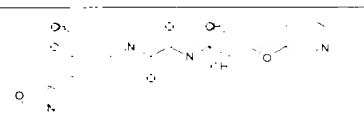
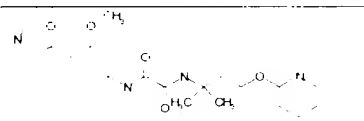
Also preferred are compounds of formulae (XVIII), and (XIVa and XIVb) where R^{12} represents aryl, a 3 to 7 membered cycloalkyl ring, or a 5 or 6 membered monocyclic or 9 or 10 membered bicyclic saturated or unsaturated heterocyclic ring with 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulfur.

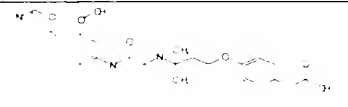

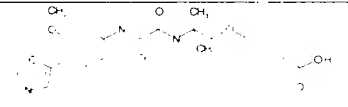
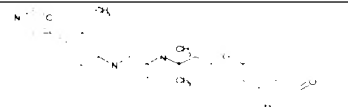
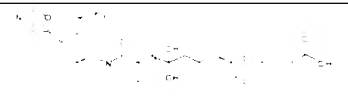
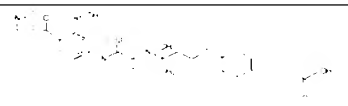
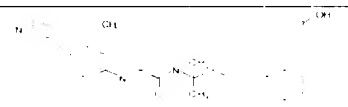
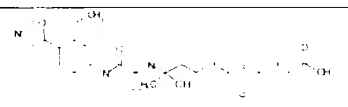
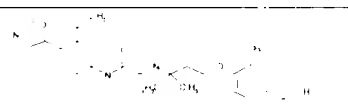
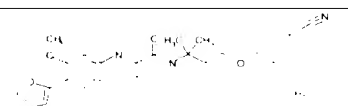
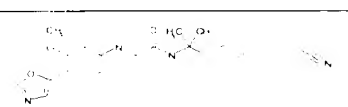

Examples of such compounds are listed in table 1f¹ below

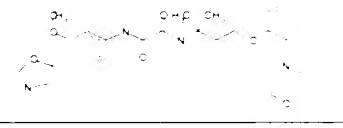
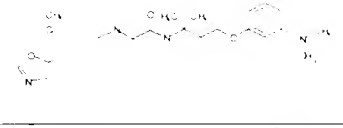
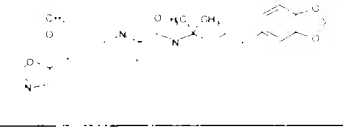
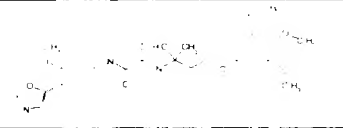
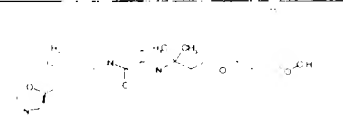
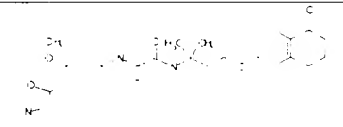
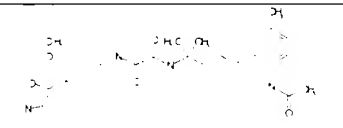
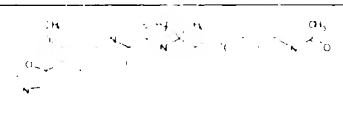
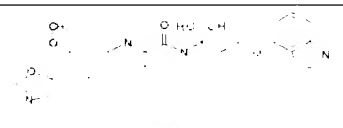
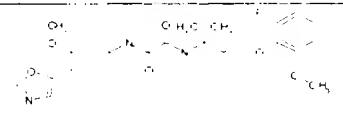
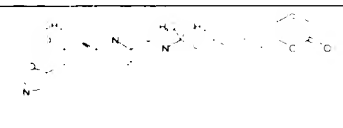
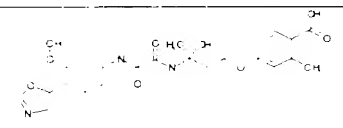
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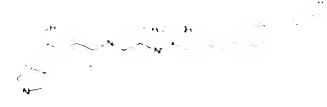
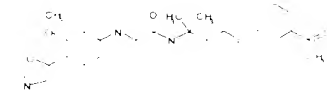
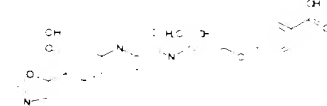
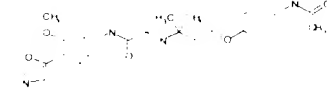
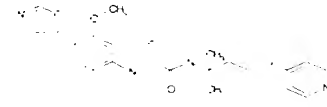
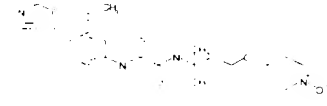
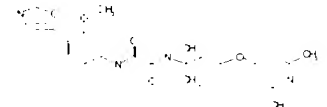
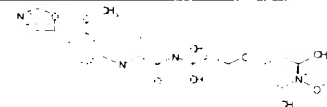
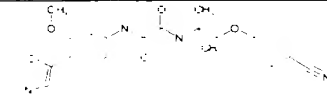
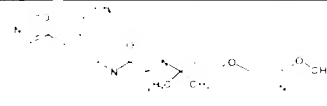
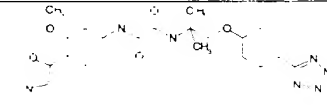
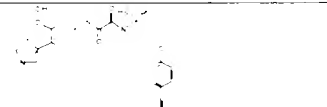
table 1f ¹			
Name	Structure	MS(ES) (M+H) ⁺	Ex No
N-[3-(4-Hydroxy-phenoxy)-1,1-dimethyl-propyl]-N'-(3-methoxy-4-oxazol-5-yl-phenyl)-oxalamide		440	396

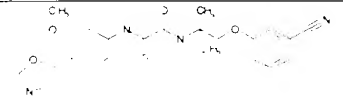
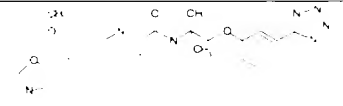
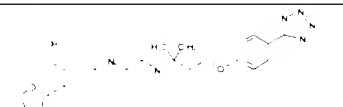
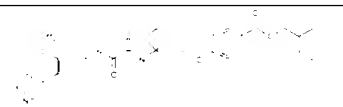
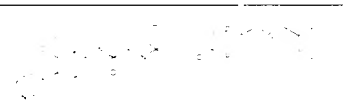
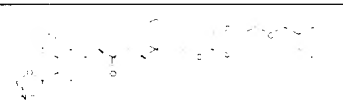
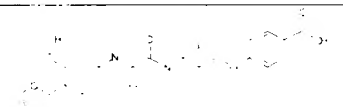
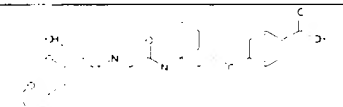
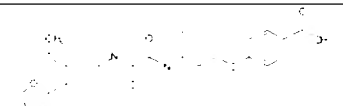
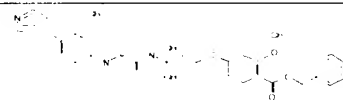
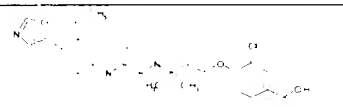
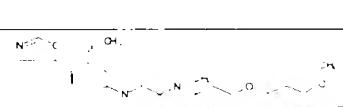
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[3-(4-methoxyphenoxy)-1,1-dimethylpropyl]oxalamide		454	397
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(4-nitrophenoxy)propyl]oxalamide		469	398
N-[3-(2-Hydroxyphenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		440	399
N-[3-(4-Amino-phenoxy)-1,1-dimethyl-propyl]-N'-(3-methoxy-4-oxazol-5-yl-phenyl)-oxalamide		439	400
N-[3-(4-Acetylamino-phenoxy)-1,1-dimethyl-propyl]-N'-(3-methoxy-4-oxazol-5-yl-phenyl)-oxalamide		481	401
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(3-pyridyloxy)propyl]oxalamide		425	402
N-[3-(3-Hydroxyphenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		440	403
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[3-(3-methoxyphenoxy)-1,1-dimethylpropyl]oxalamide		454	404
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(3-nitrophenoxy)propyl]oxalamide		469	405
N-[3-(3-Aminophenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		439	406
4-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid		468	433
2-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid		468	434

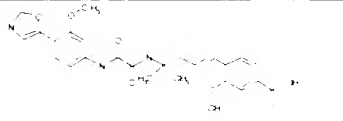

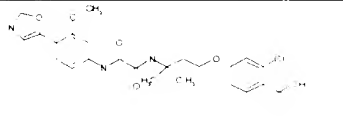
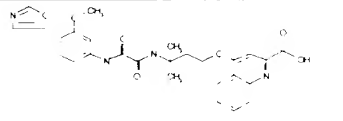
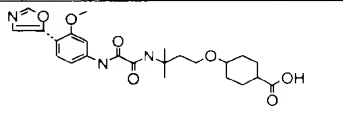
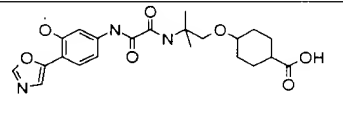
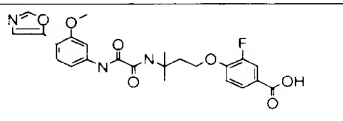
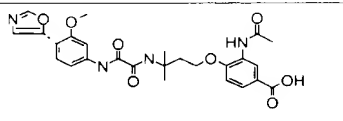
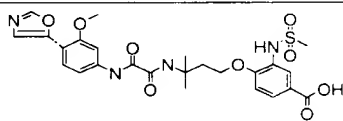
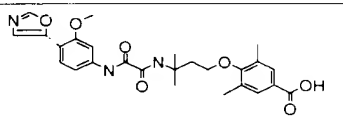
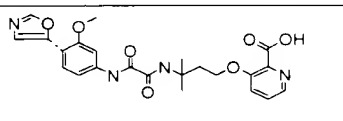
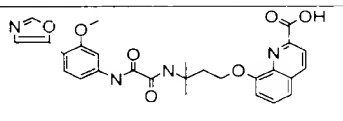
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2-[4-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]phenoxy]acetic acid		498	436
2-[2-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]phenoxy]acetic acid		498	437
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-(1,1-dimethyl-3-phenoxypropyl)oxalamide		424	542
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(1-oxido-3-pyridyloxy)propyl]oxalamide		441	543
N-[3-(3,4-Dihydroxyphenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		456	544
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-[4-(methylcarbamoyl)phenoxy]propyl]oxalamide		481	545
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[3-(3,4-dimethoxyphenoxy)-1,1-dimethylpropyl]oxalamide		484	546
N-[3-[4-[(2-Hydroxyethyl)carbamoyl]phenoxy]-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		511	547
N-[3-(3-Chlorophenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		458	548
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(3-pyridyloxy)propyl]oxalamide		425	549
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(2-pyridyloxy)propyl]oxalamide		425	550

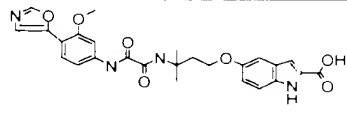
2-[4-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]phenyl]acetic acid		482	551
2-[3-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]phenyl]acetic acid		482	552
4-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropoxy]benzoic acid		454	553
4-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]-2-methylbenzoic acid		482	554
3-[3-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]phenyl]propionic acid		496	555
3-[4-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]phenyl]propionic acid		496	556
3-[2-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]phenyl]propionic acid		496	557
2-[3-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]phenoxy]acetic acid		498	558
4-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]-3-methylbenzoic acid		482	559
N-[3-(4-Cyano-2-methoxyphenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		479	560
N-[3-(3-Cyanophenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		449.6	561
N-[3-[4-(4-Acetyl-1-piperazinyl)phenoxy]-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		550.4	562

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(2-morpholinophenoxy)propyl] oxalamide		531.4 (M + Na) ⁺	563
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-[3-(dimethylamino)phenoxy]propyl] oxalamide		489.6 (M + Na) ⁺	564
N-[3-(1,3-Benzodioxol-5-yloxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl] oxalamide		468.4	565
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[3-(3,4,5-trimethoxyphenoxy)-1,1-dimethylpropyl] oxalamide		514.4	566
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[3-(3,5-dimethoxyphenoxy)-1,1-dimethylpropyl] oxalamide		506 (M + Na) ⁺	567
N-[3-(5,6,7,8-Tetrahydro-5-oxo-2-naphthyloxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl] oxalamide		492.4	568
N-[3-(2-Acetamido-5-methylphenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl] oxalamide		517.6 (M + Na) ⁺	569
N-[3-(3-Acetamidophenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl] oxalamide		503.6 (M + Na) ⁺	570
N-[3-(1H-Indol-4-yloxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl] oxalamide		485.2 (M + Na) ⁺	571
N-[3-(2-Fluoro-6-methoxyphenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl] oxalamide		472.2	572
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(2-oxo-2H-1-benzopyran-7-yloxy)propyl] oxalamide		492.4	573
N-[3-(4-Acetyl-3-methylphenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl] oxalamide		480.2	574

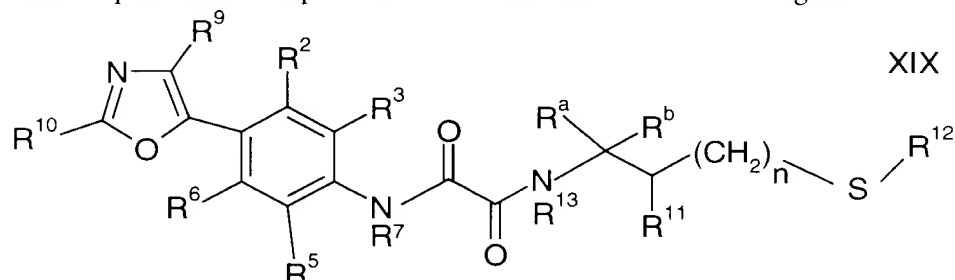
(E)-N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-[4-(3-oxo-1-butenyl)phenoxy]propyl]oxalamide		492.4	575
N-[3-(3-Acetylphenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		466.4	576
N-[3-(4-Acetylphenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		466.2	577
N-[3-(4-Acetamido-2-chlorophenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		515.6	578
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(4-pyridyloxy)propyl]oxalamide		425	579
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(1-oxido-4-pyridyloxy)propyl]oxalamide		441	580
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(2,6-dimethyl-4-pyridyloxy)propyl]oxalamide		453	581
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(2,6-dimethyl-1-oxido-4-pyridyloxy)propyl]oxalamide		469	582
N-[2-(4-Cyanophenoxy)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		435	583
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[3-(2-methoxy-4-pyridyloxy)-1,1-dimethylpropyl]oxalamide		455	584
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(1H-tetrazol-5-yl)phenoxy]ethyl]oxalamide		478	585
N-[3-(4-Cyanophenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		449	586

N-[2-(3-Cyanophenoxy)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		476	587
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[3-(1H-tetrazol-5-yl)phenoxy]ethyl]oxalamide		478	588
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-[4-(1H-tetrazol-5-yl)phenoxy]propyl]oxalamide		492	589
Benzyl 4-[2-[1-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-1-cyclobutyl]ethoxy]benzoate		570.2	590
Benzyl 4-[2-[1-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-1-cyclopentyl]ethoxy]benzoate		584.3	591
Benzyl 4-[2-[1-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-1-cyclohexyl]ethoxy]benzoate		598.3	592
4-[2-[1-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-1-cyclopentyl]ethoxy]benzoic acid		494.2	593
4-[2-[1-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-1-cyclohexyl]ethoxy]benzoic acid		508.2	594
4-[2-[1-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-1-cyclobutyl]ethoxy]benzoic acid		480.2	595
Benzyl 2-methoxy-4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoate		588	635
3-Chloro-4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid		502	636
2-Methoxy-4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid		498	637

3-Methoxy-4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid		498	638
4-[2-[1-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-1-cyclopropyl]ethoxy]benzoic acid		466	639
2-Chloro-4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid		502	640
4-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]-2-quinolinecarboxylic acid		519	641
(cis/trans)-4-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]-1-cyclohexanecarboxylic acid		474	642
(cis/trans)-4-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropoxy]-1-cyclohexanecarboxylic acid		460	643
3-Fluoro-4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid		486	644
3-Acetamido-4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid		525	645
3-(Methanesulfonamido)-4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid		561	646
4-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]-3,5-dimethylbenzoic acid		496	647
3-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]-2-pyridinecarboxylic acid		469	648
8-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]-2-quinolinecarboxylic acid		519	649

5-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]-2-indolecarboxylic acid		507	650
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Further preferred compounds of formula XVIII are those of general formula

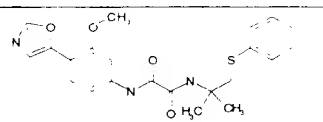
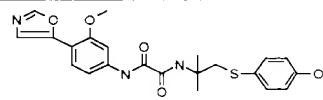
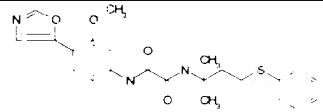
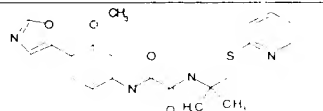


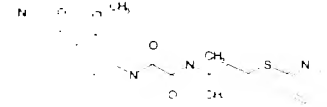
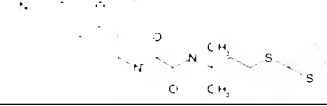
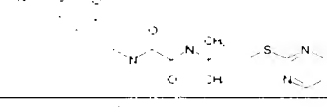
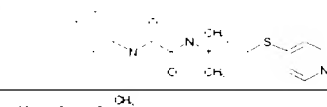
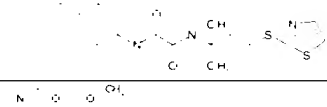
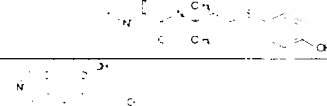
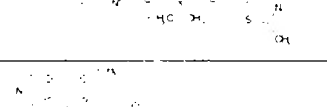
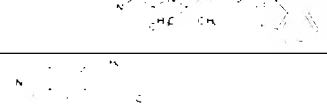
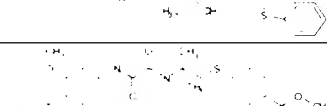
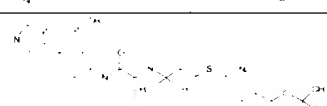
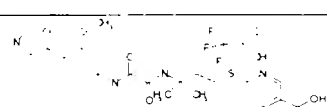
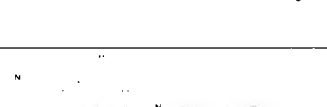
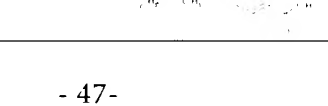
wherein R^2 , R^3 , R^5 , R^6 , R^7 , R^9 and R^{10} are defined as above, R^{11} and R^{13} are H or lower alkyl, $n=$
 0 or 1, R^a , R^b are lower alkyl or R^a and R^b taken together with the carbon atom to which they
 are attached form a 3 to 7 member carbocycle, and R^{12} is heterocyclyl, aryl or lower cycloalkyl,
 especially aryl, a 3 to 7 membered cycloalkyl ring, or a 5 to 6 membered monocyclic or 9 to 10
 membered bicyclic saturated or unsaturated heterocyclic ring with 1 to 4 heteroatoms selected
 from nitrogen, oxygen, and sulfur.

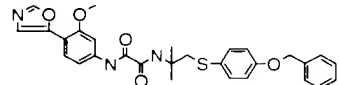
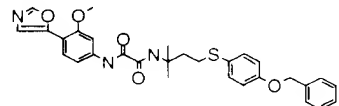
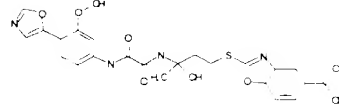
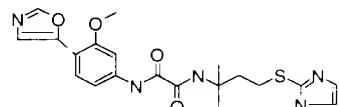
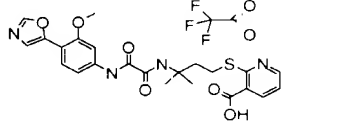
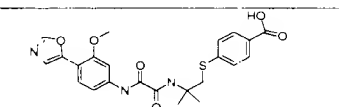
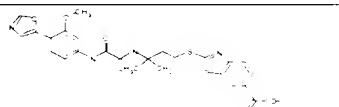
10

Particularly preferred compounds of formula (XIX) are those wherein R^2 is methoxy and R^3 ,
 R^5 , R^6 , R^9 , R^{10} , R^{11} and R^{13} are hydrogen.

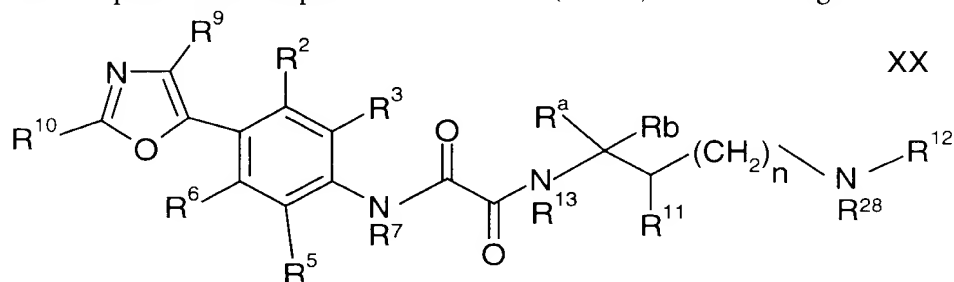
Examples of such compounds are listed in table 1f² below:

Name	Structure	MS(ES) (M+H) ⁺	Ex No
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(phenylthio)ethyl]oxalamide		426	615
N-[2-(4-Hydroxyphenylthio)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		442	616
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(phenylthio)ethyl]oxalamide		440	617
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(2-pyridylthio)ethyl]oxalamide		427	618

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(2-pyridylthio)propyl]oxalamide		441	619
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(2-thienylthio)propyl]oxalamide		446	620
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(2-pyrimidylthio)propyl]oxalamide		442	621
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(4-pyridylthio)propyl]oxalamide		441	622
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(2-thiazolylthio)propyl]oxalamide		447	623
N-[3-(4-Hydroxyphenylthio)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		456	624
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(5-methyl-1,3,4-thiadiazol-2-ylthio)propyl]oxalamide		462	625
N-[3-(2-Benzooxazolylthio)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		481	626
N-[3-(2-Benzothiazolylthio)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		497	627
Methyl 4-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropylthio]benzoate		484	628
tert-Butyl 6-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutylthio]-3-pyridinecarboxylate		541	629
6-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutylthio]-3-pyridinecarboxylic acid trifluoroacetate (1:1)		485	630
4-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutylthio]benzoic acid		484	631

N-[2-(4-Benzyloxyphenylthio)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		532	664
N-[2-(4-Benzyloxyphenylthio)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		546	665
2-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutylthio]-5-benzoxazolecarboxylic acid		525	666
N-[3-(1H-Imidazol-2-ylthio)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		430	667
2-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutylthio]-3-pyridinecarboxylic acid trifluoroacetate (1:1)		485	668
4-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropylthio]benzoic acid		470	669
2-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutylthio]-6-benzoxazolecarboxylic acid		525	670

Further preferred compounds of formula (XVIII) are those of general formula



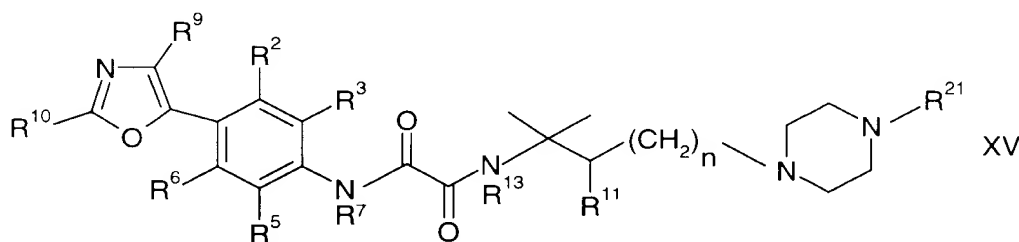
wherein $R^2, R^3, R^5, R^6, R^7, R^9$ and R^{10} are defined as above, R^{11}, R^{13} and R^{28} are H or lower alkyl, $n = 0$ or 1 , R^a, R^b are lower alkyl or R^a and R^b taken together with the carbon atom to which they are attached form a 3 to 7 number carbocycle, and R^{12} is heterocyclyl, aryl or lower cycloalkyl preferably aryl such as phenyl.

Particularly preferred compounds of formula (XX) are those wherein R^2 is methoxy and $R^3, R^5, R^6, R^9, R^{10}, R^{11}$ and R^{13} are hydrogen and R^{28} is hydrogen or methyl.

Examples of such compounds are listed in table 1f³ below.


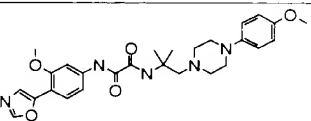
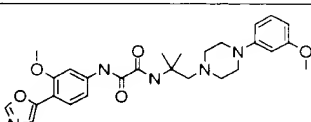
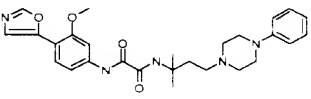
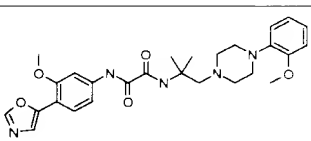
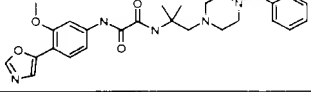
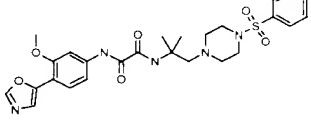
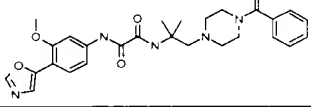
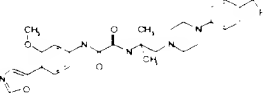
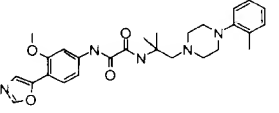
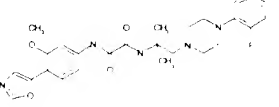
Name	Structure	MS(ES) (M+H) ⁺	Ex No
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(N-methylanilino) ethyl] oxalamide		423	632
N-(3-Anilino-1,1-dimethylpropyl)-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide hydrochloride (1:1)		423	633
4-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutylamino]benzoic acid		467	634

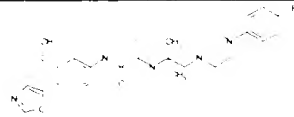
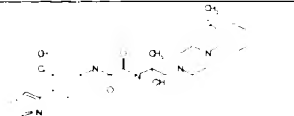
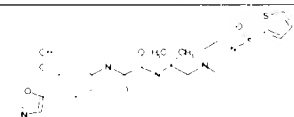
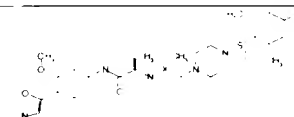
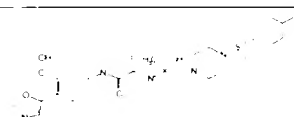
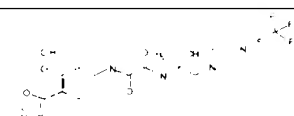
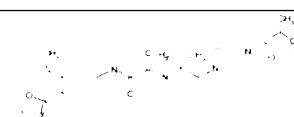
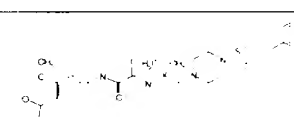
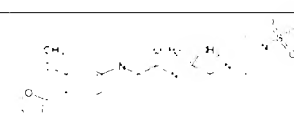
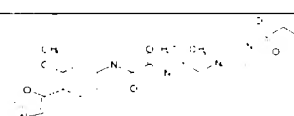
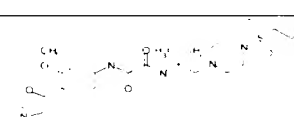
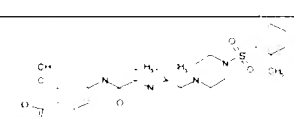
- 5 Particularly preferred compounds of formula (I) or formula (IX) are also those of general formula

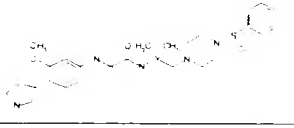

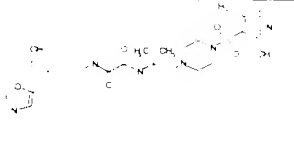
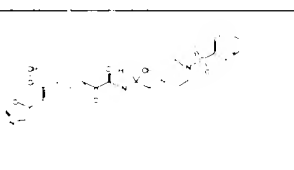
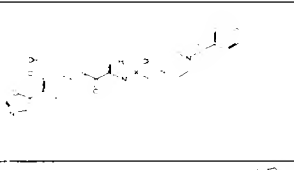
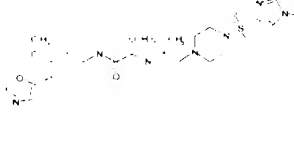
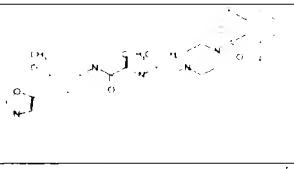
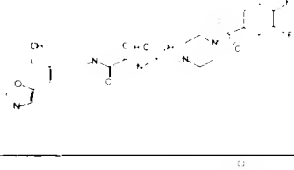
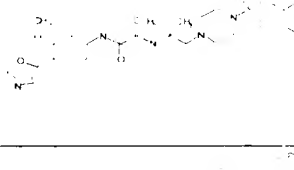
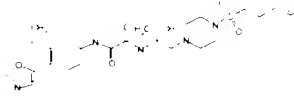



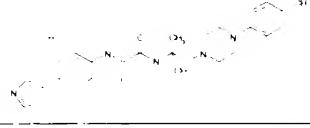
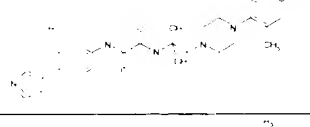
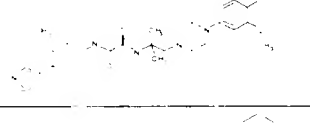
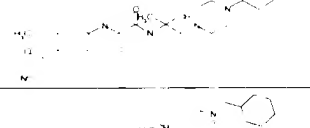
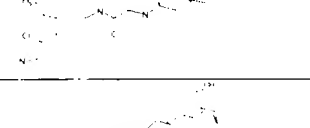
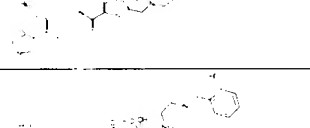
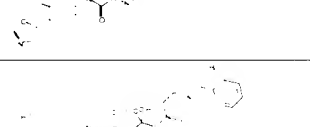
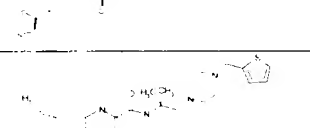
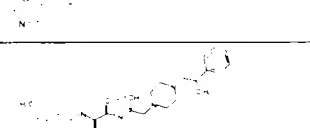
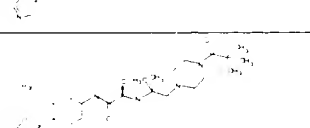
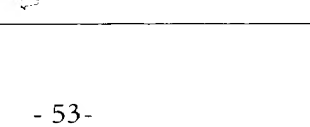
- wherein R², R³, R⁵, R⁶, R⁷, R⁹ and R¹⁰ are defined as above, R¹¹ and R¹³ is H or lower alkyl, n = 0 or 1; R²¹ is alkyl, cycloalkyl, phenyl, heterocyclyl, cycloalkyl alkyl, phenyl alkyl or heterocyclyl alkyl, alkyl carbonyl, cycloalkyl carbonyl, phenyl carbonyl, heterocyclyl carbonyl, alkyl sulphonyl, cycloalkyl sulphonyl, phenyl sulphonyl, heterocyclyl sulphonyl. Preferably R²¹ is phenyl, phenyl alkyl, phenyl carbonyl, or phenyl sulfonyl.
- 15 Particularly preferred compounds of formula (XV) are also those wherein R² is methoxy, R³, R⁵, R⁶, R⁹, R¹⁰, R¹¹ and R¹³ are hydrogen.


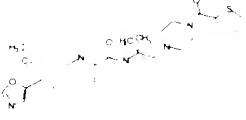
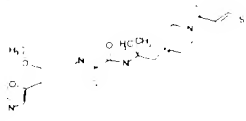
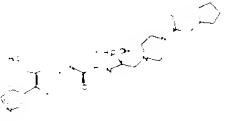
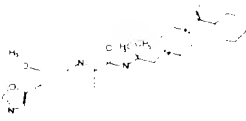
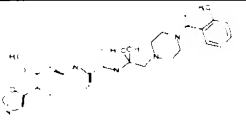
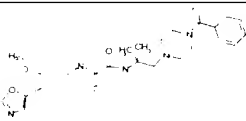
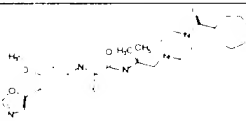
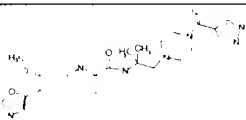
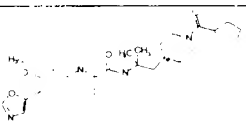
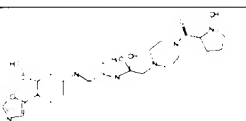
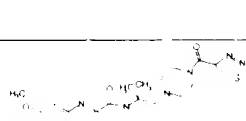
Examples of such compounds are listed in table 1g below

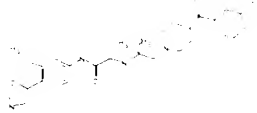

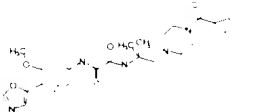
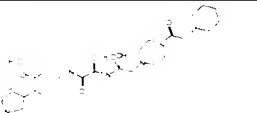

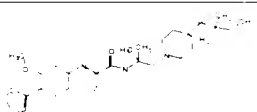
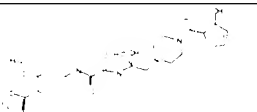
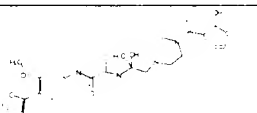
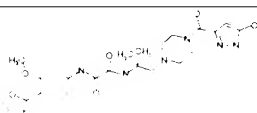
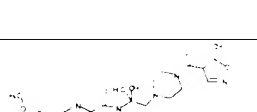

Name	Structure	MS(ES) (M+H) ⁺	Ex No
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(4-phenyl-1-piperazinyl)ethyl]oxalamide		478	407
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(4-methoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide		508	408
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(3-methoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide		508	409
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(4-phenyl-1-piperazinyl)propyl]oxalamide		492	410
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide		508	411
N-[2-(4-Benzyl-1-piperazinyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		492	412
N-[2-[4-(Benzenesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		452	413
N-[2-(4-Benzoyl-1-piperazinyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		506	414
N-[2-[4-[4-(Trifluoromethyl)phenyl]-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		546	459
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]oxalamide		492	460
N-[2-[4-(2-Fluorophenyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		496	461

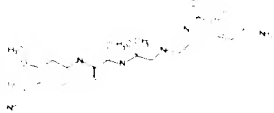
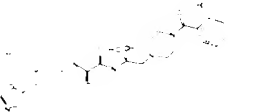
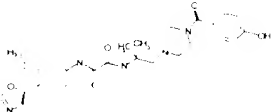
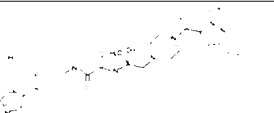
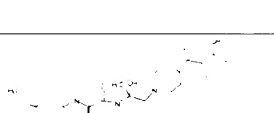
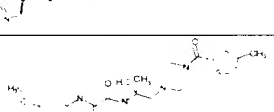
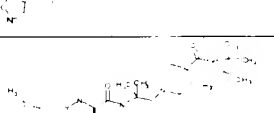

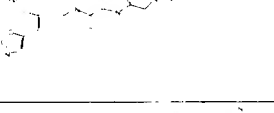
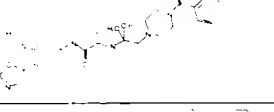

N-[2-[4-(4-Fluorophenyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		496	462
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide		508	463
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-thiophenesulfonyl)-1-piperazinyl]ethyl]oxalamide		548	464
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2,4,6-trimethylbenzenesulfonyl)-1-piperazinyl]ethyl]oxalamide		584.1	465
N-[2-[4-(4-Fluorobenzenesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		560.1	466
N-[2-[4-(Trifluoromethanesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		534	467
N-[2-[4-(Isopropylsulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		508.1	468
(E)-N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(styrylsulfonyl)-1-piperazinyl]ethyl]oxalamide		568.1	469
N-[2-[4-(Ethanesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		494.1	470
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(propanesulfonyl)-1-piperazinyl]ethyl]oxalamide		508.1	471
N-[2-[4-(3-Chloropropanesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		542.1	472
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(o-toluenesulfonyl)-1-piperazinyl]ethyl]oxalamide		556.1	473

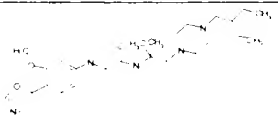
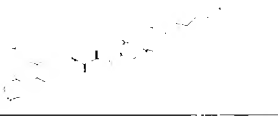
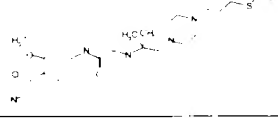
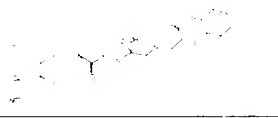
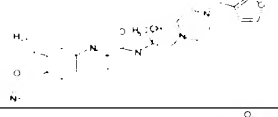
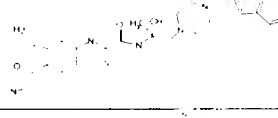
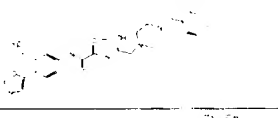
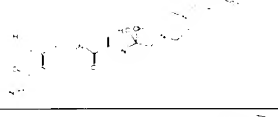
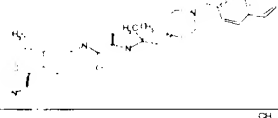
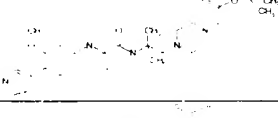
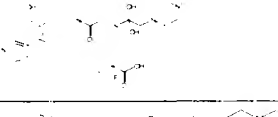
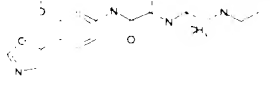
N-[2-[4-(2-Fluorobenzenesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		560.1	474
N-[2-[4-(2-Cyanobenzenesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		567.1	475
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(3,5-dimethyl-4-isoxazolylsulfonyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide		561.1	476
N-[2-[4-(5-Fluoro-2-methylbenzenesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		574.1	477
N-[2-[4-(2,5-Difluorobenzenesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		578.1	478
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(1-methyl-1H-imidazole-4-sulfonyl)-1-piperazinyl]ethyl]oxalamide		546.1	479
N-[2-[4-(2,6-Difluorobenzenesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		578.1	480
N-[2-[4-(3,4-Difluorobenzenesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		578.1	481
N-[2-[4-(Cyclohexylmethanesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		562.2	482
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-phenylethanesulfonyl)-1-piperazinyl]ethyl]oxalamide		570.1	483

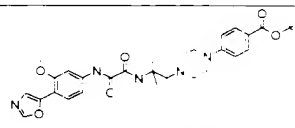
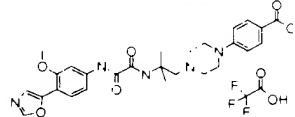
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(2,4-dimethoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide		538	484
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(4-methylphenyl)-1-piperazinyl]ethyl]oxalamide		492	485
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2,4-dimethylphenyl)-1-piperazinyl]ethyl]oxalamide		506	486
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(3,4-dimethoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide		538	487
N-[2-(4-Cyclohexyl-1-piperazinyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		484.4	488
N-[2-[4-(Cyclohexylmethyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		498.2	489
N-[2-[4-(2-Methoxybenzyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		522.1	490
N-[2-[4-(2-Hydroxybenzyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		508.1	491
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-methylbenzyl)-1-piperazinyl]ethyl]oxalamide		506.1	492
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-thenyl)-1-piperazinyl]ethyl]oxalamide		498.1	493
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2(RS)-phenylpropyl)-1-piperazinyl]ethyl]oxalamide		520.2	494
N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(4-pivaloyl-1-piperazinyl)ethyl]oxalamide		486.1	495

N-[2-[4-(2-Furoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		496.1	496
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-thenoyl)-1-piperazinyl]ethyl]oxalamide		512.1	497
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(3-thenoyl)-1-piperazinyl]ethyl]oxalamide		512	498
N-[2-[4-(2-Cyclopentylacetyl)-1-piperazinyl]-1,1-dimethyl-ethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		512.1	499
N-[2-[4-(Cyclohexylcarbonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		512.1	500
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-methylbenzoyl)-1-piperazinyl]ethyl]oxalamide		520.1	501
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(4-methylbenzoyl)-1-piperazinyl]ethyl]oxalamide		520.1	502
N-[2-[4-(Cycloheptylcarbonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		526.2	503
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(1H-pyrazol-4-yl)carbonyl]-1-piperazinyl]ethyl]oxalamide		496.1	504
N-[2-[4-(Cyclopentylcarbonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		498.1	505
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-Dimethyl-2-[4-[(1-methyl-1H-pyrrol-2-yl)carbonyl]-1-piperazinyl]ethyl]oxalamide		509.1	506
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(1,2,3-thiadiazol-4-yl)carbonyl]-1-piperazinyl]-ethyl]oxalamide		514.1	507

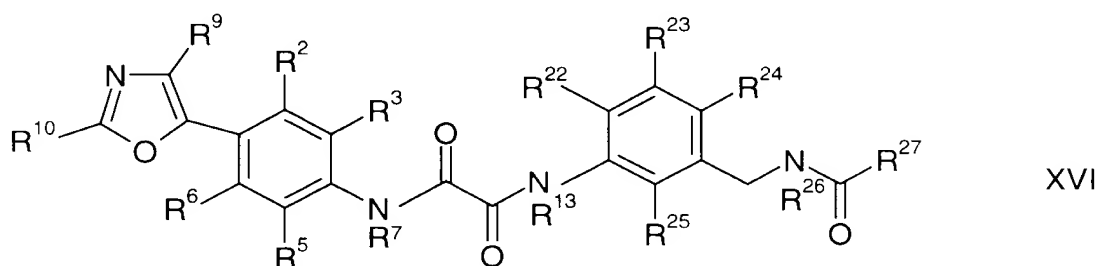
N-[2-[4-(3-Fluorobenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		524.1	508
N-[2-[4-(4-Fluorobenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		524.1	509
N-[2-[4-(Cyclopropylcarbonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		470.1	510
N-[2-[4-(2-Cyclohexylacetyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		526.2	511
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(3,3-dimethylbutyryl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide		500.2	512
N-[2-[4-(3-Hydroxy-2,2-dimethylpropionyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		502.1	513
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(3-methyl-2-furoyl)-1-piperazinyl]ethyl]oxalamide		510.1	514
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-methyl-3-furoyl)-1-piperazinyl]ethyl]oxalamide		510.1	515
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(5-methyl-1H-pyrazol-3-yl)carbonyl]-1-piperazinyl]ethyl]oxalamide		510.1	516
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(5-methyl-4-isoxazolyl)carbonyl]-1-piperazinyl]ethyl]oxalamide		511.1	517
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(5-methyl-3-isoxazolyl)carbonyl]-1-piperazinyl]ethyl]oxalamide		511.1	518

N-[2-[4-(4-Aminobenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		521.1	519
N-[2-[4-(2-Hydroxybenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		522.1	520
N-[2-[4-(4-Hydroxybenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		522.1	521
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(2,5-dimethyl-2H-pyrazol-3-yl)carbonyl]-1-piperazinyl]ethyl]oxalamide		524.1	522
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(3-methyl-2-thenoyl)-1-piperazinyl]ethyl]oxalamide		526.1	523
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(4-methyl-2-thenoyl)-1-piperazinyl]ethyl]oxalamide		526.1	524
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(2,2,3,3-tetramethyl-1-cyclopropyl)carbonyl]-1-piperazinyl]ethyl]oxalamide		526.2	525
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(4-methyl-1,2,3-thiadiazol-5-yl)carbonyl]-1-piperazinyl]ethyl]oxalamide		528.1	526
N-[2-[4-(3-Cyanobenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		531.1	527
N-[2-[4-[(Bicyclo[4.2.0]octa-1(6),2,4-trien-7-yl)carbonyl]-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		532.1	528
N-[2-[4-(3-Hydroxybenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		522.1	529

N-[2-[4-(2-Ethylbutyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		486.1	530
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-phenylethyl)-1-piperazinyl]ethyl]oxalamide		506.2	531
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[3-(methylthio)propyl]-1-piperazinyl]ethyl]oxalamide		490.1	532
N-[2-[4-(2,6-Difluorobenzyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		528.1	533
N-[2-[4-(3-Furfuryl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		482.1	534
N-[2-[4-[(2-Benzofuranyl)methyl]-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		532.1	535
N-[2-[4-(2-Cyanobenzyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		517.1	536
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(3,3-dimethylbutyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide		486.2	537
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(2-quinoliny)methyl]-1-piperazinyl]ethyl]oxalamide		543.2	538
tert-Butyl 4-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]-1-piperazineacetate		516	539
4-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]-1-piperazineacetic acid trifluoroacetate (1:1)		460	540
N-[2-[4-(Cyclopropylmethyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		456	541

tert-Butyl 4-[4-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]-1-piperazinyl]benzoate		578	651
4-[4-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]-1-piperazinyl]benzoic acid trifluoroacetate (1:1)		522	652

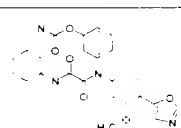
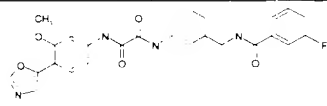
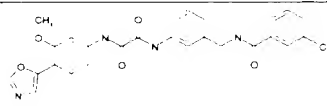
In particular preferred compounds of formula (I) and formula (IX) are also those of the general formula


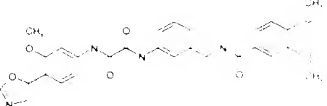
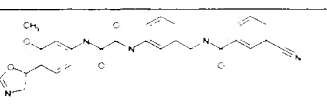


wherein $R^2, R^3, R^5, R^6, R^7, R^9, R^{10}$ and R^{13} are defined as above, $R^{22}, R^{23}, R^{24}, R^{25}$ and R^{26} are H or lower alkyl, R^{27} is alkyl, aryl or heterocyclyl, alkoxy, aryloxy, heterocyclyl oxy, especially aryl or aryloxy.

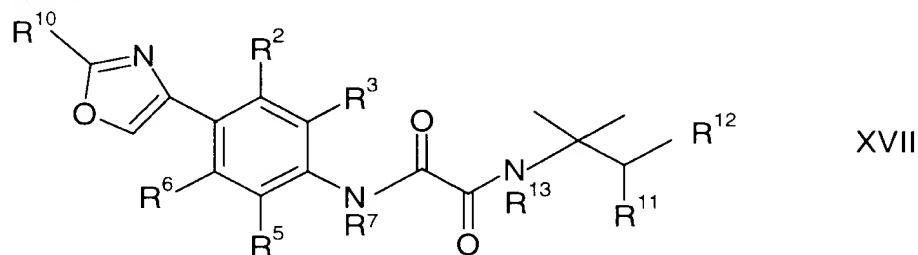
- 10 Particularly preferred compounds of formula (XVI) are those wherein R^2 is methoxy, $R^3, R^5, R^6, R^9, R^{10}, R^{13}, R^{22}, R^{23}, R^{24}, R^{25}$ and R^{26} are hydrogen.

Examples of such compounds are listed in table 1h below:

Name	Structure	ME(ES) (M+H) ⁺	Ex No
Phenyl [3-[[[4-(5-oxazolyl)anilino]oxalyl]amino]benzyl] carbamate		487	415
N-[3-[(3-Fluorobenzamido)methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		489	416
N-[3-[(3-Chlorobenzamido)methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		505	417

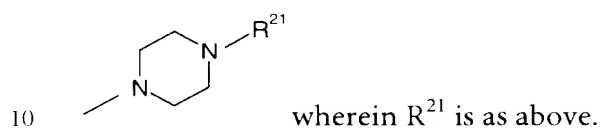
N-[3-[(3-Methoxybenzamido)methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		501.2	418
N-[3-[(3,4-Dimethoxybenzamido)methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		531.2	419
N-[3-[(3-Cyanobenzamido)methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		496.1	420

In particular preferred compounds of formula (I) or formula (IX) are also those of the general formula

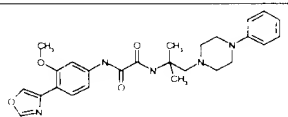


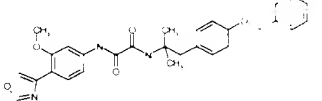
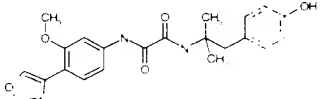
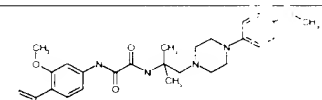
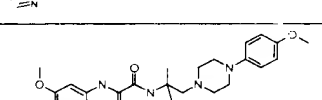
- 5 wherein R^2 , R^3 , R^5 , R^6 , R^7 and R^{10} are defined as above; R^{11} and R^{13} is H or lower alkyl and R^{12} is heterocyclyl, aryl or lower cycloalkyl.

Particularly preferred compounds of formula (XVII) are those wherein R^2 is methoxy, R^3 , R^5 , R^6 , R^9 , R^{10} , R^{11} and R^{13} are hydrogen and wherein R^{12} is phenyl or



Examples of such compounds are listed in table 1i below:

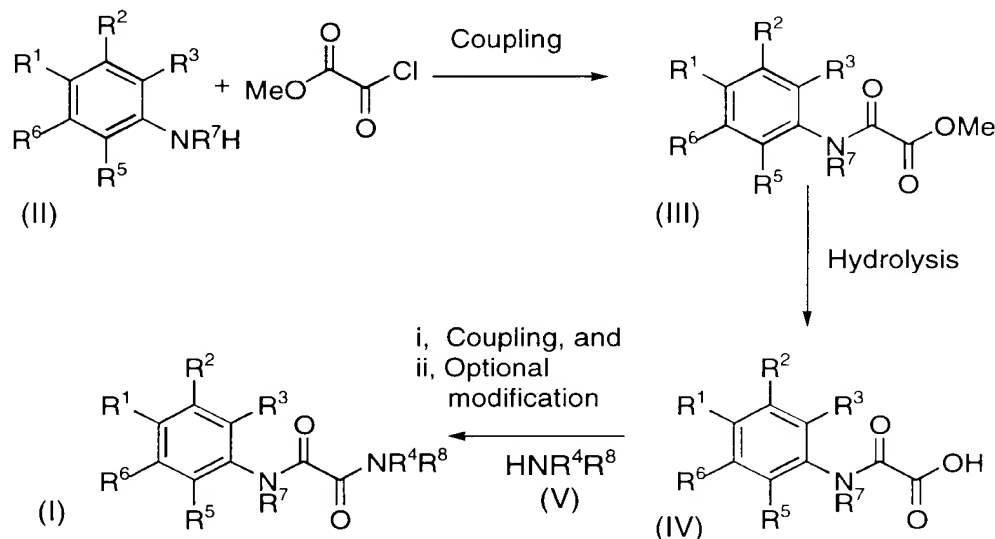
Name	Structure	MS(ES) (M+H) ⁺	Ex No
N-[3-Methoxy-4-(4-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(4-phenyl-1-piperazinyl)ethyl]oxalamide		478	428

N-[2-(4-Benzoyloxyphenyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(4-oxazolyl)phenyl]oxalamide		500	429
N-[2-(4-Hydroxyphenyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(4-oxazolyl)phenyl]oxalamide		410	430
N-[3-Methoxy-4-(4-oxazolyl)phenyl]-N'-[2-[4-(4-methoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide		508	431
N-[3-Methoxy-4-(2-methyl-4-oxazolyl)-phenyl]-N'-[2-[4-(4-methoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide		522.4	432

The compounds of formula (IV) and (VIII) which are intermediates in the foregoing processes are novel and are also provided by the present invention.

5

Reaction Scheme A



With reference to Reaction Scheme A, the first step comprises the coupling of a compound of formula (II) with an activated oxalyl derivative, such as methyl chlorooxoacetate, to give a compound of formula (III). The reaction may be carried out in a conventional manner, suitably in an organic solvent which is inert under the reaction conditions and in the presence of an organic base at about 0°C to about room temperature. Suitable solvents include halogenated

hydrocarbons, e.g. dichloromethane. Pyridine and tri(lower alkyl)amines, e.g. triethylamine, can be mentioned as examples of suitable organic bases which can be used.

Subsequent hydrolysis of the compound of formula (III) to give the acid compound of formula (IV) may be carried out by treatment with a solution of an alkali metal hydroxide, such as sodium hydroxide, in a suitable solvent system, such as aqueous methanol.

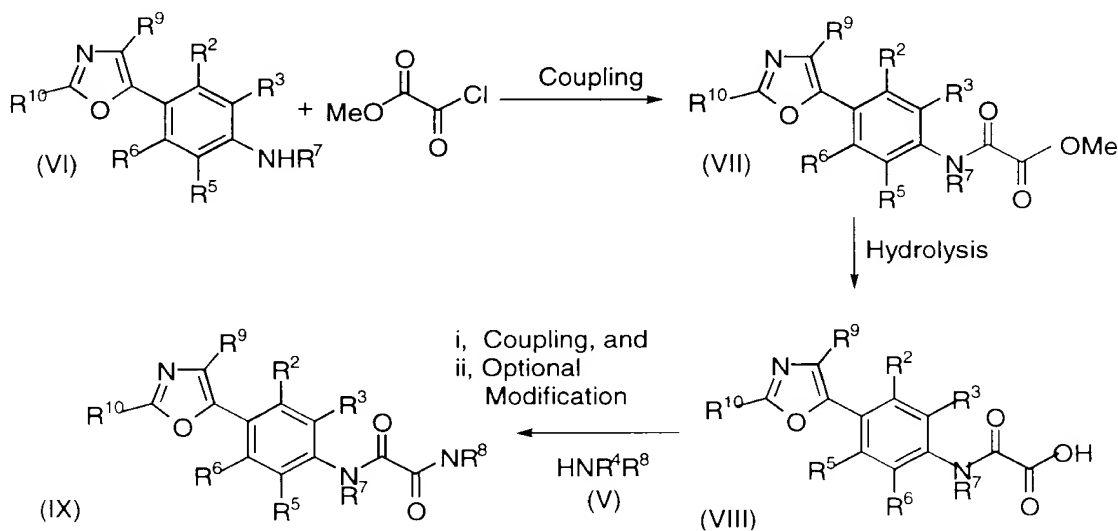
Alternatively, a compound of formula (II) may be coupled with tert.butyl chlorooxoacetate, followed by treatment with acid to remove the tert.butyl group, to give a compound of formula (IV).

The compound of formula (IV) is then coupled with an amine compound of formula (V) using standard peptide coupling reagents, such as hydroxybenzotriazole in the presence of 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride, to give the oxamide compound of formula (I).

After this coupling step, the R groups of the resulting compound may be further modified by techniques known in the art, for example, functional groups may be altered, and/or connected to further groups

20

Reaction Scheme B



Referring to Reaction Scheme B, the first step comprises the coupling of a compound of formula (VI) with an activated oxalyl derivative, such as methyl chlorooxoacetate, to give a compound of formula (VII). The reaction is carried out in the manner described above for the formation of a compound of formula (III) from a compound of formula (II).

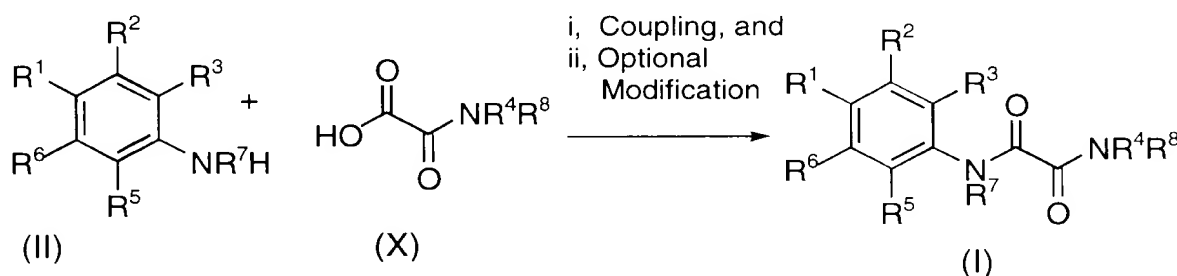
Subsequent hydrolysis of the compound of formula (VII) to give the acid compound of formula (VIII) is then carried out as described above for the hydrolysis of a compound of formula (III).

Alternatively, a compound of formula (VI) may be coupled with tert.butyl chlorooxoacetate, followed by treatment with acid to remove the tert.butyl group, to give a compound of formula (VIII).

The compound of formula (VIII) is then coupled with an amine compound of formula (V) to give the oxamide compound of formula (IX), under the conditions described above for the coupling of a compound of formula (IV) with a compound of formula (V).

After this coupling step, the R groups of the resulting compound may be further modified by techniques known in the art, for example, functional groups may be altered, and/or connected to further groups

Reaction Scheme C



Alternatively, compounds of formula (I) are made by the coupling of a compound of formula (II) with an oxalamic acid compound of formula (X), using standard peptide coupling reagents,

such as hydroxybenzotriazole in the presence of 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride, to give the oxamide compound of formula (I).

After this coupling step, the R groups of the resulting compound may be further modified by techniques known in the art, for example, functional groups may be altered, and/or connected to further groups

As mentioned above, the compounds of formula (I) and salts thereof are inhibitors of IMPDH enzyme both in vitro and in vivo, and can be used in the control or prevention of IMPDH mediated conditions or diseases.

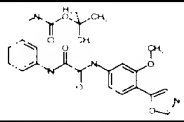
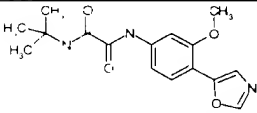
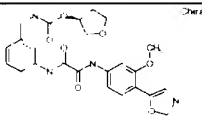

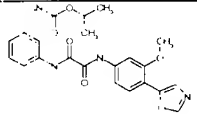
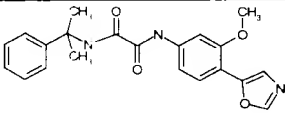
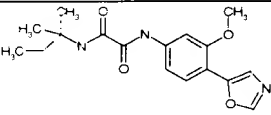
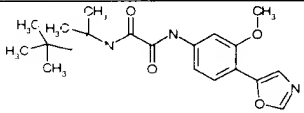
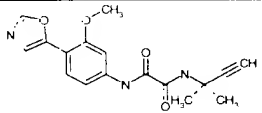
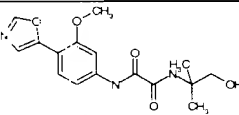
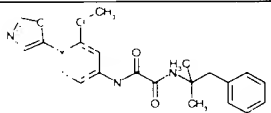
IMPDH activity can be assayed using an adaptation of the method reported by Carr [S. Carr et al., J. Biol. Chem. 268, p.27286 (1993)], the disclosure of which is herein incorporated by reference. IMPDH activity was measured spectrophotometrically, by monitoring the increase in absorbance at 340nm due to the formation of NADH (ϵ_{340} is $6220 \text{ M}^{-1} \text{ cm}^{-1}$) from the reduction of NAD. The IMPDH reaction mixture contained 0.1M Tris pH8.0, 0.1M KCl, 1mM DTT, 3mM EDTA, 100mM IMP and 100mM NAD. The reaction was initiated by the addition of IMPDH (human type II) to a final concentration in the assay of between 1nM and 5nM with respect to the IMPDH tetramer. The initial rate is measured by following the linear increase in absorbance at 340nm at 37°C for 45 minutes. The reading was conducted using a Spectromax 190 (Molecular Devices) spectrophotometer in a 96 well plate format with a final reaction volume of 200 μ l.


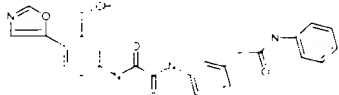
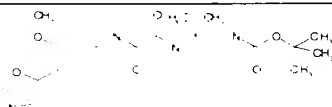
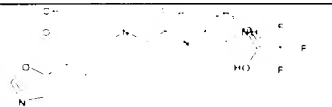
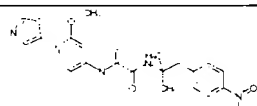
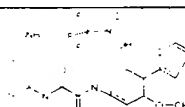
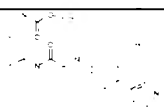
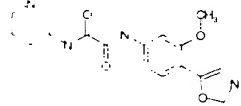
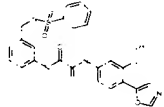
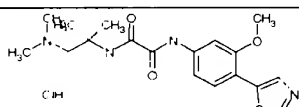
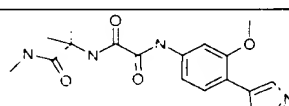
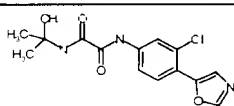
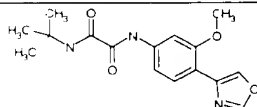
For inhibitor assay analysis, the compound is dissolved in DMSO to a final concentration of 10mM and added to the initial reaction mixture as 5 μ l to give final DMSO concentration of 2.5%. The enzyme reaction is initiated by the addition of IMPDH and the initial rates measured as above. IC_{50} determinations are made by measuring the initial rates in the presence of 10 concentrations of inhibitor and fitting the data using the 4 parameter curve fit from the Softmax pro software (Molecular Devices).

Preferred compounds of the invention tested in the above assay have an IC_{50} value up to 500nM i.e. 0.5 μ M.

Specific examples of IC₅₀ values for preferred compounds of formula (I) are set out below in Table 2:

Table 2

Compound of Formula (I)	IC ₅₀ (μM)
	0.036
	0.037
	0.044
	0.013
	0.033
	0.03
	0.031
	0.034
	0.048
	0.072
	0.015

	Phenyl [3-[[[4-(5-oxazolyl)anilino]oxalyl]amino]benzyl] carbamate	0.011
	N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[3-[(phenylcarbamoyl)methyl]phenyl]oxalamide	0.035
	tert-Butyl [2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl] carbamate	0.075
	N-(2-Amino-1,1-dimethylethyl)-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide trifluoroacetate (1:1)	0.097
	N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(4-nitrophenyl)ethyl]oxalamide	0.010
	N-[3-(Aminomethyl)phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide trifluoroacetate (1:1)	0.233
	Methyl [3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]benzyl] carbamate	0.121
	N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-(3-pyridyl)oxalamide	0.277
	N-[3-[(Benzenesulfonamido)methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide	0.125
	N-(2-Dimethylamino-1,1-dimethylethyl)-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide hydrochloride (1:1)	0.17
	N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1-methyl-1-(methylcarbamoyl)ethyl]oxalamide	0.199
	N-tert-Butyl-N'-[3-chloro-4-(5-oxazolyl)phenyl]oxalamide	0.169
	N-tert-Butyl-N'-[3-methoxy-4-(4-oxazolyl)phenyl]oxalamide	0.46

Compounds of formula (I) which are acidic can form pharmaceutically acceptable salts with bases such as alkali metal hydroxides, e.g. sodium hydroxide and potassium hydroxide; alkaline earth metal hydroxides, e.g. calcium hydroxide, barium hydroxide and magnesium hydroxide, and the like; with organic bases e.g. N-ethyl piperidine, dibenzylamine, and the like.

5 Those compounds of formula (I) which are basic can form pharmaceutically acceptable salts with inorganic acids, e.g. with hydrohalic acids such as hydrochloric acid and hydrobromic acid, sulphuric acid, nitric acid and phosphoric acid, and the like, and with organic acids, e.g. with acetic acid, tartaric acid, succinic acid, fumaric acid, maleic acid, malic acid, salicylic acid, citric acid, methanesulphonic acid and p-toluene sulphonic acid, and the like. The formation
10 and isolation of such salts can be carried out according to methods known in the art.

The oxamide derivatives provided by the present invention (i.e. the compounds of formula (I) and their pharmaceutically acceptable salts, especially as depicted in all the formulae herein), can be used as medicaments, for example in the form of pharmaceutical preparations. The
15 pharmaceutical preparations can be administered enterally, such as orally, in the form of tablets, coated tablets, dragées, hard and soft gelatine capsules, solutions, emulsions or suspensions, or nasally, e.g. in the form of nasal sprays. They can also be administered rectally, e.g. in the form of suppositories, or parenterally, (e.g. intramuscularly, intravenously, or subcutaneously), for example, in the form of injection solutions.

20 For the manufacture of pharmaceutical preparations the oxamide derivatives can be formulated with therapeutically inert, inorganic or organic carriers. Lactose, corn starch or derivatives thereof, talc, stearic acid or its salts can be used, for example, as such carriers for tablets, coated tablets, dragées and hard gelatine capsules. Suitable carriers for soft gelatine
25 capsules are, for example, vegetable oils, waxes, fats, semi-solid and liquid polyols and the like. Depending on the nature of the active ingredient no carriers are, however, generally required in the case of soft gelatine capsules. Suitable carriers for the manufacture of solutions and syrups are, for example, water, polyols, sucrose, saccharose, invert sugar, glucose and the like. Suitable carriers for the manufacture of injection solutions are, for example, water, saline,
30 alcohols, polyols, glycerine, vegetable oils and the like. Natural or hardened oils, waxes, fats, semi-liquid or liquid polyols and the like are suitable carriers for the manufacture of suppositories. The pharmaceutical preparations of the present invention may also be provided as sustained release formulations or other appropriate formulations.

The pharmaceutical preparations can also contain preservatives, solubilizers, stabilizers, wetting agents, emulsifiers, sweeteners, colourants, flavourants, salts for adjustment of the osmotic pressure, buffers, masking agents or antioxidants. They may also contain other therapeutically active substances, such as an immunosuppressant, a chemotherapeutic agent, an anti-viral agent, an antibiotic, an anti-parasitic agent, an anti-fungal agent, an anti-inflammatory agent and/or an anti-vascular hyperproliferation agent. A preferred agent that may be used with the compounds of the present invention is interferon or derivatives thereof, such as conjugates with polyethylene glycol.

10

Accordingly part of this invention is a pharmaceutical composition comprising a compound of formula (I) or its pharmaceutically acceptable salt and a pharmaceutically acceptable carrier, and, optionally, one or more additional therapeutically active substance(s). Such substances may be one or more immunosuppressants, chemotherapeutic agents, antivirals, antibiotic, antiparasitics, antifungals, antiinflammatories, or antivascular antiproliferation agents. Preferably the substance is interferon or an interferon derivative.

15

Medicaments containing compounds of formula (I) or salts thereof and a therapeutically acceptable carrier, as well as a process for the manufacture of such medicaments are also objects of the present invention. This process comprises bringing a compound of formula (I) or a pharmaceutically acceptable salt thereof into a galenical administration form together with a therapeutically inert carrier material and, if desired, one or more additional therapeutically active substances.

20

A further object of the invention comprises the use of the oxamide derivatives provided by the invention in the treatment of an immune mediated condition or disease, a viral disease, a bacterial disease, a parasitic disease, inflammation, an inflammatory disease, a hyperproliferative vascular disease, a tumour, or cancer. The dosage can vary within wide limits and will, of course, be adjusted to the individual requirements in each particular case. Dosage levels of between about 0.01 and about 100 mg/kg body weight per day (preferably 0.5 - 75 mg/kg/day) in monotherapy and/or in combination therapy are preferred, administered from about 1 - 5 times per day. The active ingredient may be combined with a carrier material. A typical preparation will contain from about 5% - 95% active compound (w/w) (preferably

30

from about 20% - 80% active compound). The daily dosage can be administered as a single dosage or in divided dosages.

Accordingly this invention is also directed to a method for treating an immune mediated
5 condition or disease, a viral, bacterial, parasitic, inflammatory ,hyperproliferative vascular
disease, inflammation, a tumor, or cancer in a subject by administering to the subject a
therapeutically effective amount of a compound of formula (I) or its pharmaceutically
acceptable salts. In addition, this method includes concurrent or sequential administration of
one or more therapeutically active substances taken from immunosuppresants,
10 chemotherapeutics, antivirals, antibiotics, antiparasitics, antifungals, antiinflammatories, and
anti-vascular hyperproliferation agents. Preferably the substance is interferon or an interferon
derivative.

This invention is especially directed to a method for treating IMPDH mediated diseases.
15

The compounds and compositions of the present invention may be for use in monotherapy
and/or combination therapy, i.e. the treatment may be in conjunction with the administration
of one or more additional therapeutically active substance(s). When the treatment is
combination therapy, such administration may be concurrent or sequential with respect to that
20 of the oxamide derivatives of the present invention. Thus, concurrent administration, as used
herein, includes administration of the agents in conjunction or combination, together, or
before or after each other.

It will be understood that references herein to treatment extend to prophylaxis as well as to
25 treatment of existing conditions. Treatment of a disease or condition, as used herein, also
includes preventing, inhibiting, regressing, reversing, alleviating or relieving the disease or
condition, or the clinical symptoms thereof. The term "subject" as used herein refers to
animals, including humans and other mammals.

30 The following Examples illustrate the present invention.

With regard to the starting materials that are known compounds some of these may be
purchased from commercial suppliers. Other starting materials that are known and their

analogues can be prepared by methods well known in the art. Examples of compounds available from commercial suppliers, and citations to the synthesis of other compounds and their analogues are provided in the following:

- 5 Compounds of formula (II) and the compounds of formula (VI) are obtained from commercial suppliers (e.g. 4-(5-oxazolyl)aniline, Maybridge catalogue number DFP 00120), or prepared by adaptation of the methods disclosed in published patent application WO 974002, or prepared by adaptation of the methods provided in Palacz et al., FEBS Lett., 1984, 176(2), 365-370.

10

The compounds of formula (V) are obtained from commercial suppliers (e.g. tert-butylamine, Aldrich catalogue number B8,920-5; Cumylamine, TCI-US catalogue number C1293), or prepared by adaptation of the methods provided in Kazuo Achiwa et al., Chem.Pharm.Bull., 1998, 46(4), 697-670.

15

The compounds of formula (X) are prepared by adaptation of the methods provided in Minisci et al., J. Org. Chem., 1995, 60(17), 5430-5433.

20

Examples of commercially available reagents include those used in Examples 7, 10 and 11, (2-methoxy-4-nitrobenzoic acid, Aldrich catalogue number 42,291-6; tert-butylacetic acid, Aldrich catalogue number B8,840-3; and p-tolualdehyde, Aldrich catalogue number T3,560-2, respectively).

25

Where indicated, the NMR spectra were recorded on a Bruker DRX 400 MHz spectrometer with the probe temperature set at 300 K.

30

Where indicated by "(M⁺;EI)", mass spectra were recorded under electron impact conditions (EI), on a THERMOQUEST MAT95 S with a source temperature of 200°C. Other mass spectra were recorded under electrospray ionisation spectra (ESI) conditions, on one of the following machines:

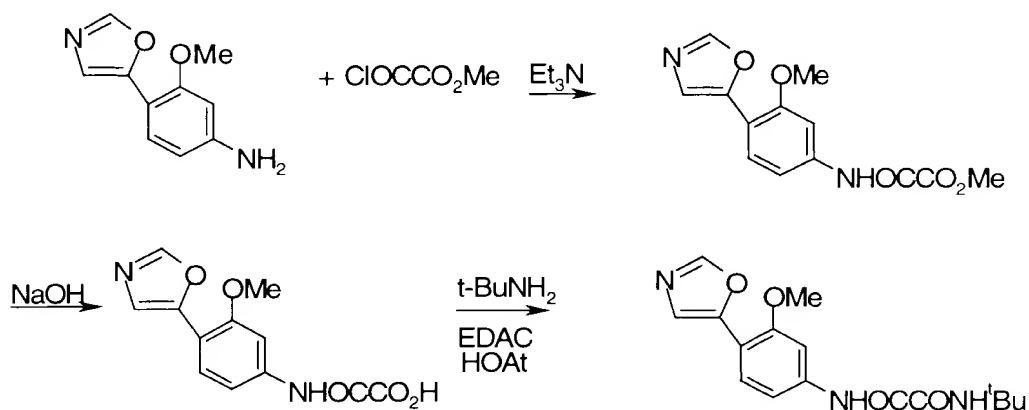
a) THERMOQUEST SSQ 7000 [Solvent 0.085% TFA in 90% Acetonitrile/water; flow rate 100 microliters/minute; capillary 250°C; spray voltage 5KV; sheath gas 80 psi], or

b) LC-MS system (liquid chromatograph coupled to mass spectrum) THERMOQUEST TSQ 7000 ELECTROSPRAY or MICROMASS PLATFORM ELECTROSPRAY [Solvent 0.1% TFA in water or 0.085% TFA in 90% acetonitrile/ water or 0.085% TFA in acetonitrile].

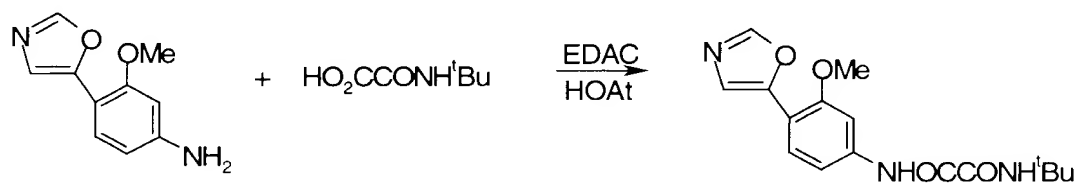
- 5 Unless otherwise indicated, the mass spectroscopy values recorded in the MS(ES) column refer to $(M+H)^+$ values, apart from the ones shown as $(M^+;EI)$.

Example 1

- 10 N-Tert-butyl-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide



Example 1, Alternative synthesis



- 15 A solution of 26 mg (0.1 mmol) of N-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamic acid, 15 mg (0.2 mmol) of tertiary butylamine, 28 mg (0.15 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride and 15 mg (0.11 mmol) of 1-hydroxy-7-azabenzotriazole in 1 ml of dimethylformamide was stirred at room temperature for 4 hours then diluted with ethyl acetate and washed with 2M hydrochloric acid, saturated sodium bicarbonate and water.
- 20 The resulting solution was dried over magnesium sulphate and evaporated to dryness. The residue was triturated with diethyl ether/petrol (1:1) and collected by filtration to give 11 mg of

N-tert-butyl-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide as a white solid. MS: m/e 318.0 [M+H]⁺.

The starting material was prepared as follows:

5

i) 5.7 g (30 mmol) of 3-methoxy-4-(5-oxazolyl)aniline and 3.33 g (33 mmol) of triethylamine were dissolved in 50 ml of dichloromethane and the solution was cooled to 0°C. A solution of 3.86 g (31.5 mmol) of methyl oxalyl chloride in 10 ml of dichloromethane was added dropwise and the resulting mixture was stirred for 1 hour then washed with 2M hydrochloric acid. The precipitated solid was collected by filtration and washed with dichloromethane and water to give 6.2 g of methyl N-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamate as a yellow solid. ¹H NMR (400 MHz, DMSO-d₆) δ: 3.88 (3H,s), 3.94 (3H,s), 7.48 (1H,s), 7.58 (1H,dd), 7.65 (1H,d), 7.68 (1H,d), 8.39 (1H,s), 10.92 (1H,s).

15 ii) 6.2 g (22.46 mmol) of methyl N-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamate and 1.2 g (30 mmol) of sodium hydroxide were refluxed in 240 ml of methanol/water (1:1) for 2 hours then cooled, filtered and acidified with 2M hydrochloric acid. The precipitated solid was collected by filtration and washed with water, acetone and diethyl ether to give 5.1 g of N-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamic acid as a pale yellow solid. MS: m/e 262.9 [M+H]⁺.

20

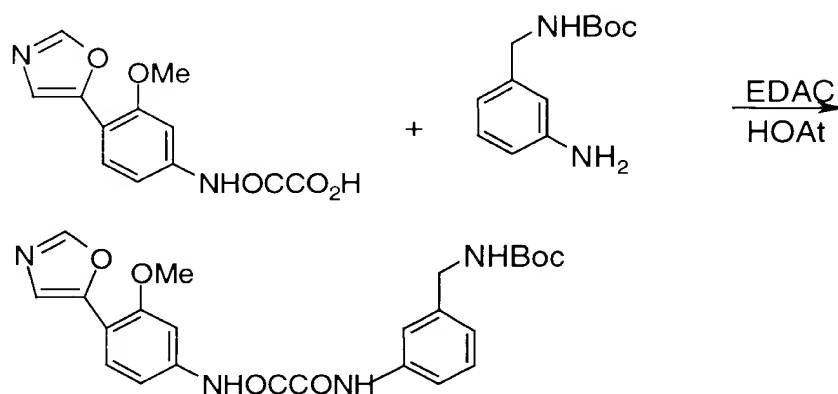
Alternatively N-tert-butyl-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide can be prepared as follows:

A solution of 95 mg (0.5 mmol) of 3-methoxy-4-(5-oxazolyl)aniline, 73 mg (0.5 mmol) of N-tert-butyloxalamic acid, 134 mg (0.7 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride and 75 mg (0.55 mmol) of 1-hydroxy-7-azabenzotriazole in 4 ml of dichloromethane was stirred at room temperature for 18 hours. The resulting mixture was washed with 2M hydrochloric acid and saturated sodium bicarbonate, dried over magnesium sulphate and evaporated to dryness. The residue was triturated with petrol and collected by filtration to give 128 mg of N-tert-butyl-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide as a pale yellow solid. MS: 318 [M+H]⁺.

30

Example 2

Tert-butyl [3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl] amino]benzyl]carbamate

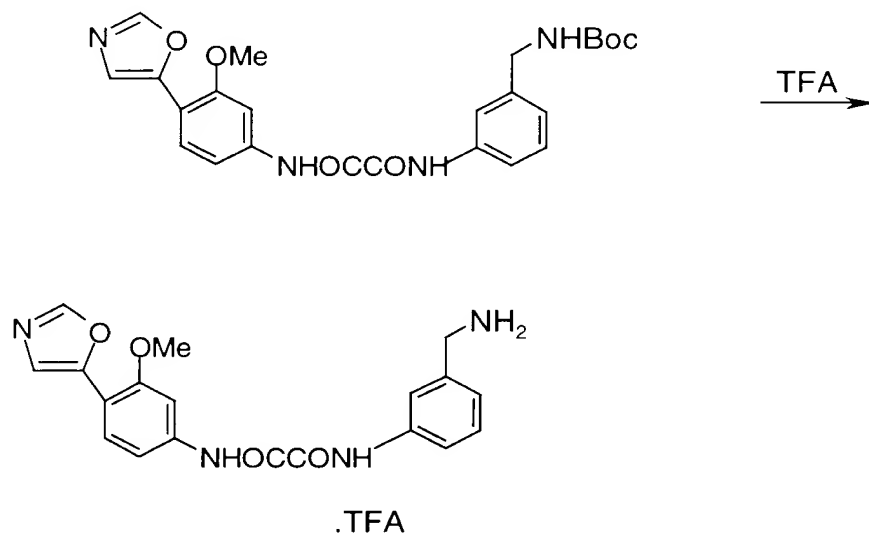


10 A mixture of 2.04 g (7.79 mmol) of N-(3-methoxy-4-(5-oxazolyl)phenyl)oxalamic acid, prepared as described above in Example 1 above, 1.9 g (8.56 mmol) of tert-butyl (3-aminobenzyl)carbamate, 1.8 g (9.4 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride and 1.3 g (9.6 mmol) of 1-hydroxy-7-azabenzotriazole in 30 ml of dimethylformamide was stirred for 20 hours at room temperature. The resulting precipitate was collected by filtration and washed with dichloromethane to give 1.8 g of tert-butyl [3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]benzyl]carbamate as a white solid. MS: m/e 466 M⁺.

15

Example 3

N-[3-(Aminomethylphenyl)-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide trifluoroacetate

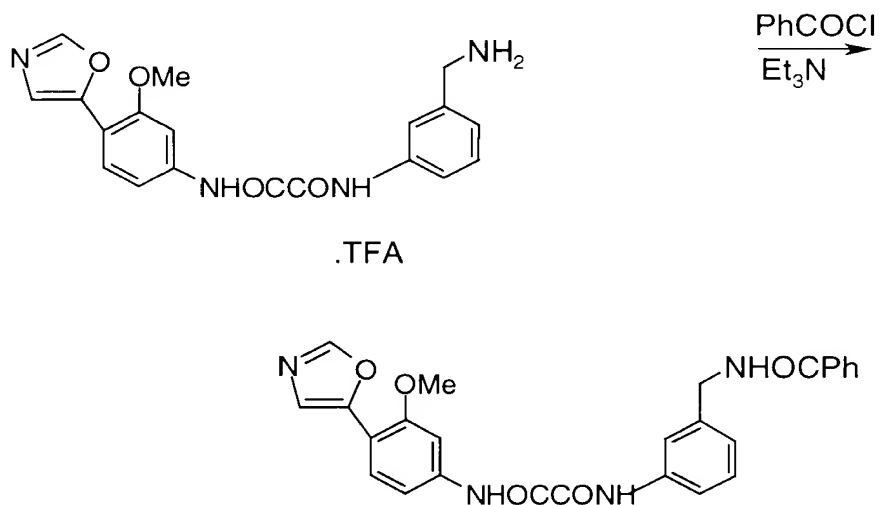


5

15 mg (0.032 mmol) of tert-butyl [3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]-amino]benzyl]carbamate, prepared as described in Example 2 above, were dissolved in 1 ml of dichloromethane and 1 ml of trifluoroacetic acid at room temperature for 5 minutes. The solution was evaporated to dryness, the residue triturated with diethyl ether and collected by
10 filtration to give 11 mg of N-[3-(aminomethylphenyl)-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide trifluoroacetate as a white solid. MS: m/e 408 [M+H+MeCN]⁺.

Example 4

N-[3-(Benzamidomethyl)phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide



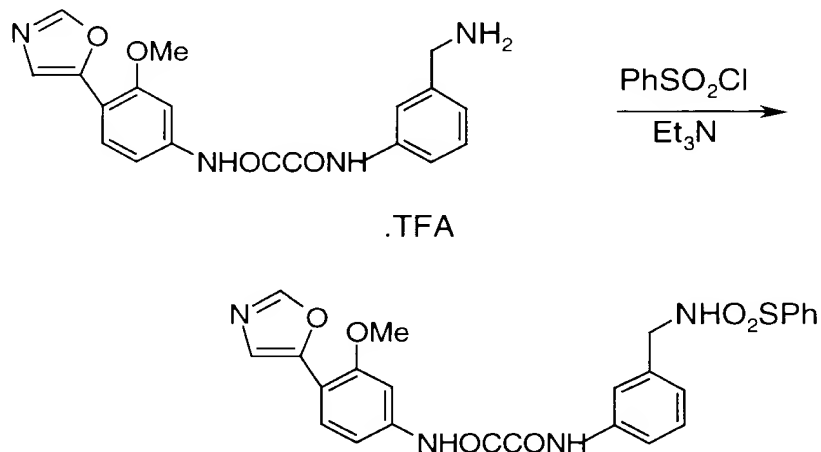
5

29 mg (0.21 mmol) of benzoyl chloride were added to a solution of 100 mg (0.21 mmol) of N-[3-(aminomethyl)phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl] oxalamide trifluoroacetate, prepared as described in Example 3 above, and 46 mg (0.46 mmol) of triethylamine in a mixture of 2 ml of dimethylformamide and 5 ml of dichloromethane, and stirred at room temperature for 18 hours. The solution was washed with 2M hydrochloric acid and saturated sodium bicarbonate then dried over magnesium sulphate and evaporated to dryness. The residue was chromatographed on silica gel using ethyl acetate/petrol (2:1) for the elution. After trituration with diethyl ether there was obtained 45 mg of N-[3-(benzamidomethyl)phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide as a white solid. MS: m/e 471.0 [M+H]⁺.

Example 5

N-[3-[(Benzenesulphonamido)methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide

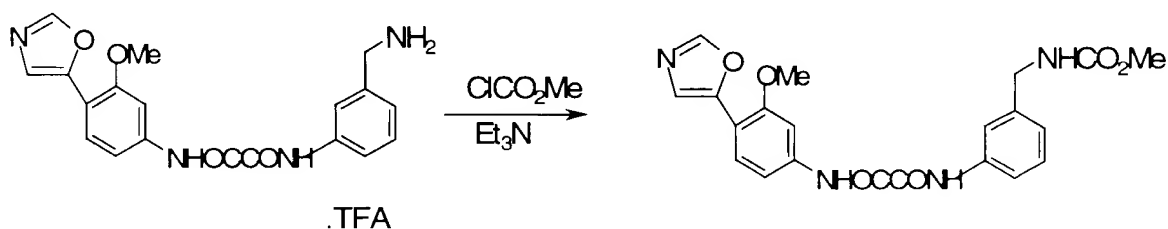
5



In an analogous manner to that described in Example 4 but replacing benzoyl chloride with phenylsulphonyl chloride there was obtained N-[3-[(benzenesulphonamido)methyl]-
 10 phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide as a white solid. MS: m/e 507 [M+H]⁺.

Example 6

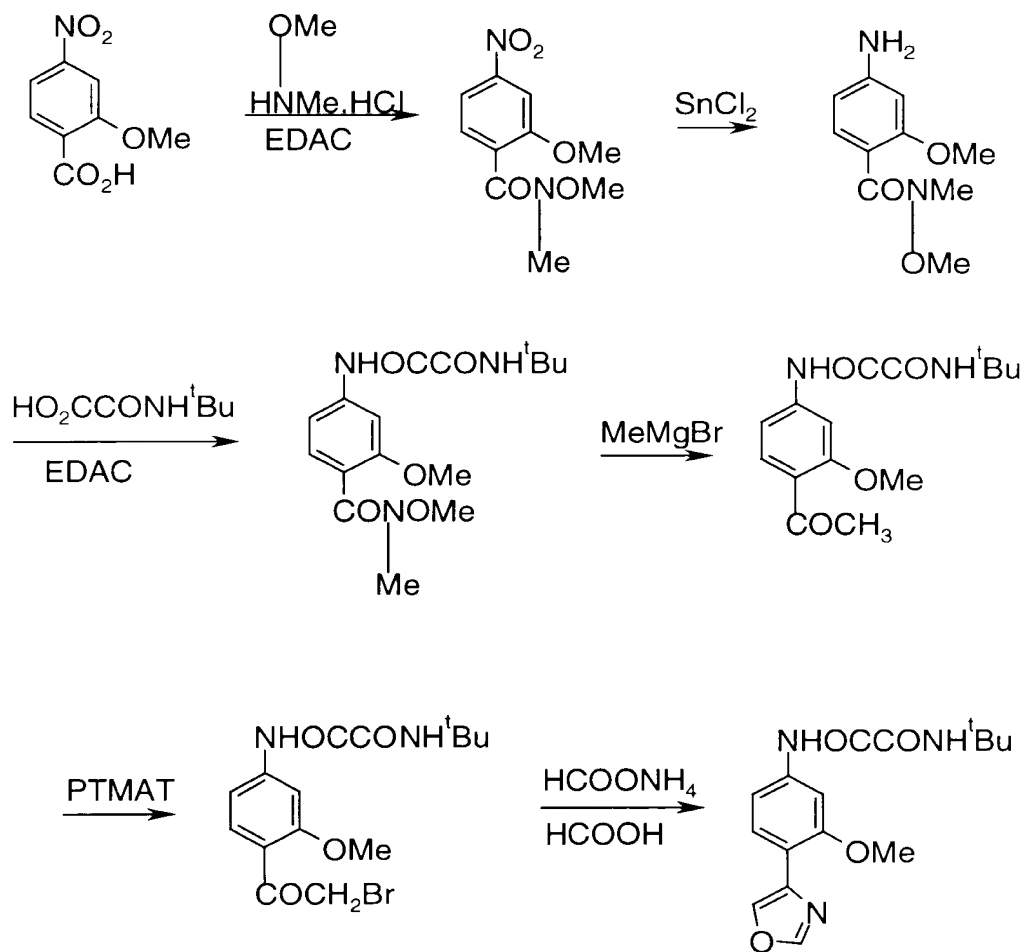
15 Methyl [3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxazolyl]aminobenzyl]carbamate



In an analogous manner to that described in Example 4 but replacing benzoyl chloride with methyl chloroformate there was obtained methyl [3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]benzyl]carbamate as a white solid. MS: m/e 425 [M+H]⁺.

5 Example 7

N-Tert-butyl-N'-[3-methoxy-4-(4-oxazolyl)phenyl]oxalamide



- 10 A mixture of 371 mg (1 mmol) of N-[4-(bromoacetyl)-3-methoxyphenyl]-N'-tert-butylloxalamide and 315 mg (5 mmol) of ammonium formate was refluxed in 10 ml of formic acid for 4 hours then cooled and evaporated to dryness. The residue was dissolved in ethyl

acetate, washed with 2M sodium hydroxide and dried over magnesium sulphate. The solution was evaporated to dryness and the residue chromatographed on silica gel using ethyl acetate/petrol (7:18) for the elution. There was obtained after trituration with diethyl ether/petrol (1:1) 65 mg of N-tert-butyl-N'-[3-methoxy-4-(4-oxazolyl)phenyl]oxalamide as a white solid. MS: m/e 318 [M+H]⁺.

The starting material was prepared as follows:

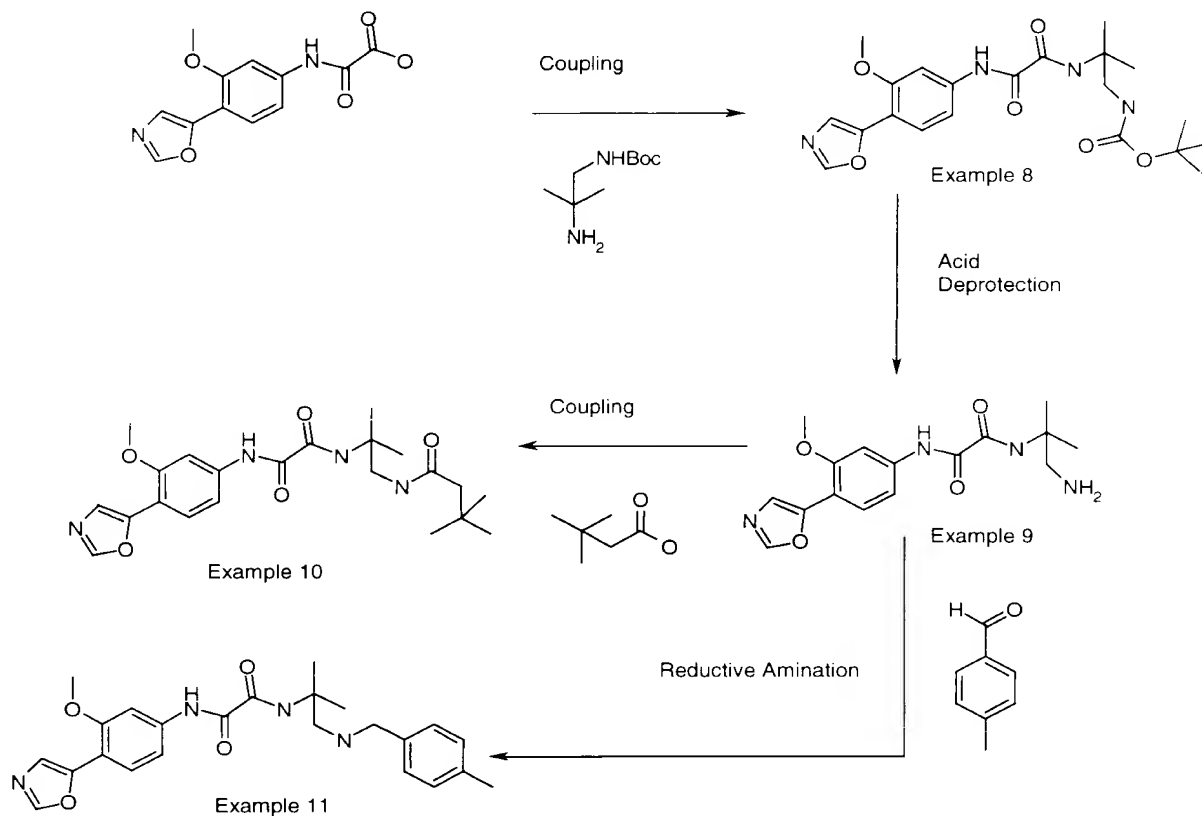
- i) A mixture of 3.94 g (20 mmol) of 2-methoxy-4-nitrobenzoic acid, 3.9 g (40 mmol) of N,O-dimethylhydroxylamine hydrochloride, 5.73 g (29.92 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride, 3.37 g (22 mmol) of 1-hydroxybenzotriazole hydrate and 5.06 g (44 mmol) of N-ethylmorpholine in 50 ml of dichloromethane was stirred at room temperature for 3 hours then washed with 2M hydrochloric acid and saturated bicarbonate. The resulting solution was dried over magnesium sulphate, evaporated to dryness and the residue triturated with diethyl ether and collected by filtration to give 3.95 g of N,O-dimethyl 2-methoxy-4-nitrobenzohydroxamate as a white solid. ¹H NMR (400 MHz, CDCl₃) δ: 3.37 (3H,s), 3.48 (3H,s), 3.97 (3H,s), 7.45 (1H,d), 7.80 (1H,d), 7.91 (1H,dd).
- ii) A mixture of 1.2 g (5 mmol) of N,O-dimethyl 2-methoxy-4-nitrobenzohydroxamate and 4.75 g (25 mmol) of tin(II) chloride in 40 ml of ethanol was heated at 80°C for 30 minutes then cooled and evaporated to dryness. The residue was dissolved in dichloromethane, washed with 2M sodium hydroxide and the organic phase dried over magnesium sulphate and evaporated to dryness to give 960 mg of N,O-dimethyl 4-amino-2-methoxybenzohydroxamate as an off-white solid. ¹H NMR (400 MHz, CDCl₃) δ: 3.25 (3H,s), 3.62 (3H,s), 3.79 (3H,s), 6.22 (1H,d), 6.28 (1H,dd), 7.09 (1H,d).
- iii) A mixture of 700 mg (3.33 mmol) of N,O-dimethyl 4-amino-2-methoxybenzohydroxamate, 483 mg (3.33 mmol) of N-tert-butyloxalamic acid, 600 mg (3.92 mmol) of 1-hydroxybenzotriazole hydrate and 960 mg (5.01 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride in 15 ml of dichloromethane was stirred at room temperature for 3 hours then washed with 2M hydrochloric acid and saturated sodium bicarbonate. The organic phase was dried over magnesium sulphate, evaporated to

dryness and the residue chromatographed on silica gel using ethyl acetate/petrol (3:1) for the elution to give 960 mg of N,O-dimethyl 4-[[[(tert-butylamino)oxalyl] amino]-2-methoxybenzohydroxamate as a white solid. ¹H NMR (400 MHz, CDCl₃) δ: 1.46 (9H,s), 3.25-3.4 (3H,br.s.), 3.45-3.65 (3H,br.s.), 3.89 (3H,s), 7.08 (1H,dd), 7.29 (1H,d), 7.44 (1H,s), 7.53 (1H,d), 9.40 (1H,s).

iv) 3.1 ml (4.34 mmol) of 1.4M methylmagnesium bromide in tetrahydrofuran were added in portions over 1 hour to a solution of 337 mg (1 mmol) of N,O-dimethyl 4-[[[(tert-butylamino)oxalyl]amino]-2-methoxybenzohydroxamate in 10 ml of anhydrous tetrahydrofuran. The resulting solution was diluted with diethyl ether and washed with 2M hydrochloric acid. The organic phase was dried over magnesium sulphate, evaporated to dryness and the residue chromatographed on silica gel using ethyl acetate/petrol (3:7) for the elution to give 255 mg of N-(4-acetyl-3-methoxyphenyl)-N'-tert-butyloxalamide as a white solid. ¹H NMR (400 MHz, CDCl₃) δ: 1.45 (9H,s), 2.61 (3H,s), 3.96 (3H,s), 7.03 (1H,dd), 7.43 (1H,s), 7.64 (1H,d), 7.82 (1H,d), 9.47 (1H,s).

v) 320 mg (0.85 mmol) of phenyltrimethylammonium tribromide were added in portions over 10 minutes to a stirred solution of 247 mg (0.85 mmol) of N-(4-acetyl-3-methoxyphenyl)-N'-tert-butyloxalamide in 5 ml of anhydrous tetrahydrofuran. After 15 minutes a further 100 mg (0.26 mmol) of phenyltrimethylammonium tribromide were added. The resulting suspension was diluted with diethyl ether, washed with water and the organic phase was dried over magnesium sulphate. Evaporation gave a gum which was chromatographed on silica gel using firstly 0.5% methanol in dichloromethane then 1% methanol in dichloromethane for the elution. The product was dissolved in diethyl ether/petrol (2:1) and the resulting crystals were collected by filtration to give 135 mg of N-[4-(bromoacetyl)-3-methoxyphenyl]-N'-tert-butyloxalamide as a white solid. ¹H NMR (400 MHz, CDCl₃) δ: 1.44 (9H,s), 3.99 (3H,s), 4.61 (2H,s), 7.06 (1H,dd), 7.42 (1H,s), 7.68 (1H,d), 7.93 (1H,d), 9.51 (1H,s).

Examples 8-11



5 Example 8

Tert-butyl[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]carbamate

77mg (0.87 mmol) of tert-butyl (2-amino-2-methylpropyl)carbamate , 207 mg
 10 (1.05 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride, 166 mg
 (1.08 mmol) of 1-hydroxy-7-azabenzotriazole and 200 mg (0.76 mmol) of N-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamic acid were dissolved in 5 ml of dichloromethane and 5 ml of dimethylformamide and stirred for 16 hours at room temperature. The mixture was then diluted with 50 ml of dichloromethane and washed with a 10% solution of citric acid and
 15 brine. The organic layer was then dried with anhydrous magnesium sulphate, filtered and evaporated to dryness. The residue was chromatographed on silica gel using 30% ethyl acetate in hexane for the elution to give 165 mg of tert-butyl [2-[[[3-methoxy-4-(5-oxazolyl)-

anilino]oxalyl]amino]-2-methylpropyl]carbamate as a yellow solid, ¹H NMR (400MHz, d₆ DMSO) δ: 1.35 (s, 6H), 1.45 (s, 9H), 3.25 (d, 2H), 3.95 (s, 3H), 7.25 (t, 1H), 7.55 (s, 1H), 7.70 (m, 2H), 7.80 (s, 1H), 8.25 (s, 1H), 8.50 (s, 1H), 10.8 (s, 1H).

5 Example 9

N-(2-Amino-1,1-dimethylethyl)-N'-[3-methoxy-4-(5-oxazolyl)phenyl]
oxalamide trifluoroacetate (1:1)

10 26 mg (0.29 mmol) of tert-butyl [2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]carbamate was dissolved and stirred in 10 ml of a 1:1 mixture of 1,1,1-trifluoroacetic acid and dichloromethane. After 1 hour the solvent mixture was co-evaporated with toluene three times and dichloromethane twice. The resulting gum was then triturated with 40-60 petroleum ether to give 124 mg of N-(2-amino-1,1-
15 dimethylethyl)-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide trifluoroacetate (1:1) as a yellow solid, ¹H NMR (400MHz, d₆ DMSO) δ: 1.40 (s, 6H), 3.20 (m, 2H), 3.90 (s, 3H), 7.50 (s, 1H), 7.60-7.74 (m, 2H), 7.80 (s, 1H), 7.90 (s(br), 3H), 8.30 (s, 1H), 8.40 (s, 1H), 10.80 (s, 1H).

The previously described trifluoroacetic acid salt was partitioned between a saturated
20 sodium hydrogencarbonate solution and ethyl acetate. The organic layer was then dried with magnesium sulphate, filtered and evaporated to give the free base used in Example 10.

Example 10

25 N-(3-Methoxy-4-(5-oxazolyl)phenyl)-N'-[2-(3,3-dimethylbutyramido)-1,1-dimethylethyl]oxalamide

30 30 mg (0.09 mmol) of N-(2-amino-1,1-dimethyl-ethyl)-N'-(3-methoxy-4-oxazol-5-yl-phenyl)-oxalamide, 52 mg (0.45 mmol) of tert-butylacetic acid, 86 mg (0.45 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride and 69 mg of HOAt were dissolved and stirred in 2 ml of dimethylformamide. After stirring for 16 hours the mixture was diluted with 10 ml of dichloromethane and washed with 10% citric acid solution in water, saturated sodium hydrogen carbonate solution and brine. The organic solution was then dried with solid

magnesium sulphate, filtered and evaporated to give N-(3-methoxy-4-(5-oxazolyl)phenyl)-N'-[2-(3,3-dimethylbutyramido)-1,1-dimethylethyl]oxalamide as a pale yellow solid, MS: m/e 431.3 [M+H]⁺

5 Example 11

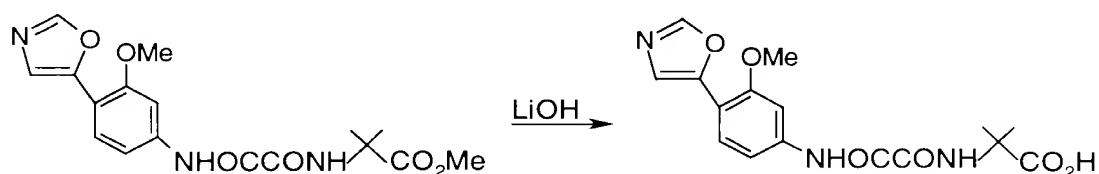
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-(4-methylbenzylamino)-1,1-dimethylethyl]oxalamide

10 30 mg (0.09 mmol) of N-(2-amino-1,1-dimethyl-ethyl)-N'-(3-methoxy-4-oxazol-5-yl-phenyl)-oxalamide, 11.3 mg (0.095 mmol) of 4-methylbenzaldehyde and 30 mg (0.14 mmol) of sodium triacetoxyborohydride were dissolved in 2ml of a 5% acetic acid dichloromethane mixture for 16 hours. The reaction mixture was then diluted with 8 ml of dichloromethane and washed with water, saturated sodium hydrogen carbonate and brine. The resulting organic
15 solution was then dried with magnesium sulphate, filtered and evaporated to give N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[2-(4-methylbenzylamino)-1,1-dimethylethyl]oxalamide as a yellow solid MS: m/e 437.3 [M+H]⁺.

Example 12

20

2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropionic acid



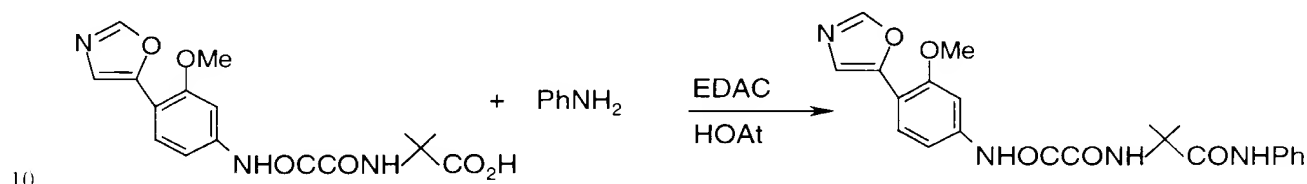
25 A mixture of 161 mg (0.446 mmol) of methyl 2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropionate and 56 mg (1.33 mmol) of lithium hydroxide hydrate in 3 ml of methanol and 0.5 ml of water was heated at 50°C for 2 hours then diluted with water and washed with diethyl ether. The aqueous phase was acidified to pH2 with 2M hydrochloric acid and extracted twice with ethyl acetate. The combined organic
30 extracts were dried over magnesium sulphate and evaporated to dryness. The residue was

chromatographed on silica gel using dichloromethane/methanol/acetic acid/water (120:15:3:2) for the elution. After trituration with ether there was obtained 70 mg of 2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropionic acid as a white solid. MS: m/e 247.9 [M+H]⁺.

5

Example 13

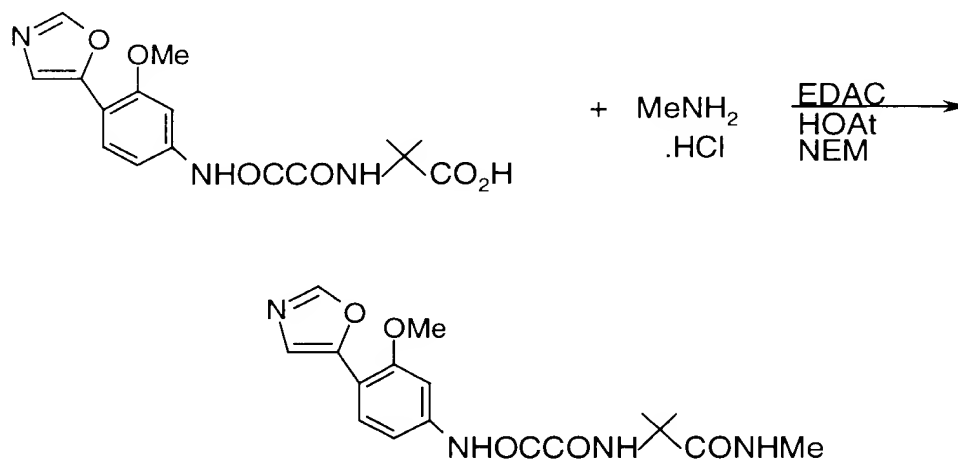
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1-methyl-1-(phenylcarbamoyl)ethyl]oxalamide



A solution of 30 mg (0.086 mmol) of 2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropionic acid, 16 mg (0.172 mmol) of aniline, 15 18 mg (0.132 mmol) of 1-hydroxy-7-azabenzotriazole and 25 mg (0.131 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride in 2 ml of dimethylformamide was stirred at room temperature for 18 hours then diluted with ethyl acetate and washed with 2M hydrochloric acid and saturated sodium bicarbonate. The organic phase was dried over magnesium sulphate and after evaporation the residue was trituated with diethyl ether and 20 collected by filtration to give 20 mg of N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[1-methyl-1-(phenylcarbamoyl)ethyl]oxalamide as a white solid. MS: m/e 423.0 [M+H]⁺.

Example 14

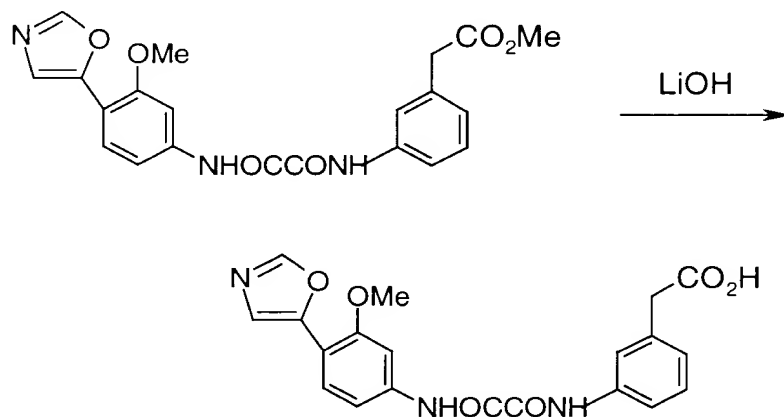
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1-methyl-1-(methylcarbamoyl)ethyl]oxalamide



A mixture of 30 mg (0.086 mmol) of 2-[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropionic acid, 12 mg (0.178 mmol) of methylamine hydrochloride, 18 mg (0.132 mmol) of 1-hydroxy-7-azabenzotriazole, 25 mg (0.131 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride and 22 mg (0.218 mmol) of triethylamine in 2 ml of dimethylformamide was stirred at room temperature for 18 hours then diluted with ethyl acetate and washed with 2M hydrochloric acid and saturated sodium bicarbonate. The organic solution was dried over magnesium sulphate, evaporated to dryness and the residue chromatographed on silica gel using dichloromethane/methanol (24:1) for the elution. After trituration with ether there was obtained 17 mg of N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[1-methyl-1-(methylcarbamoyl)ethyl]oxalamide as a white solid. MS: m/e 361.0 [M+H]⁺.

Example 15

2-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]phenyl]acetic acid



5

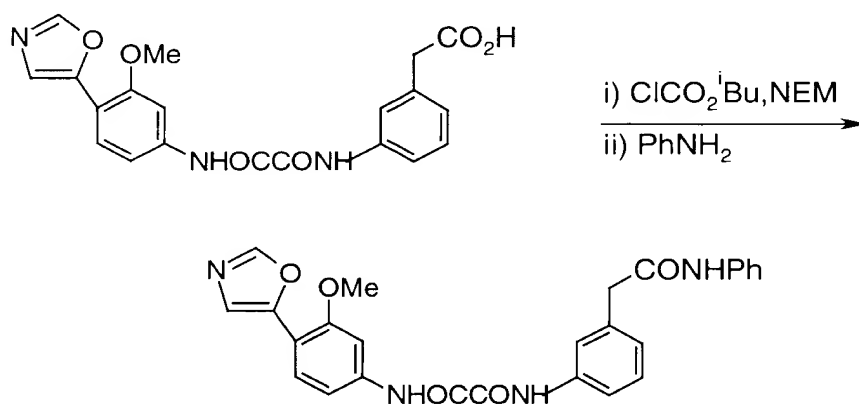
A solution of 740 mg (1.81 mmol) of methyl 2-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]phenyl]acetate and 152 mg (3.62 mmol) of lithium hydroxide hydrate in 10 ml of methanol, 10 ml of 1,4-dioxane and 5 ml of water was stirred at room temperature for 18 hours. The solvent was removed by evaporation and the residue dissolved in water. The aqueous solution was washed with diethyl ether and acidified with citric acid solution. The solid which precipitated was collected by filtration and washed with water, ethanol and diethyl ether to give 414 mg of 2-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]phenyl]acetic acid as a white solid. MS: m/e 396.0 [M+H]⁺.

15

Example 16

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[3-[(phenylcarbamoyl)methyl]phenyl]oxalamide

5

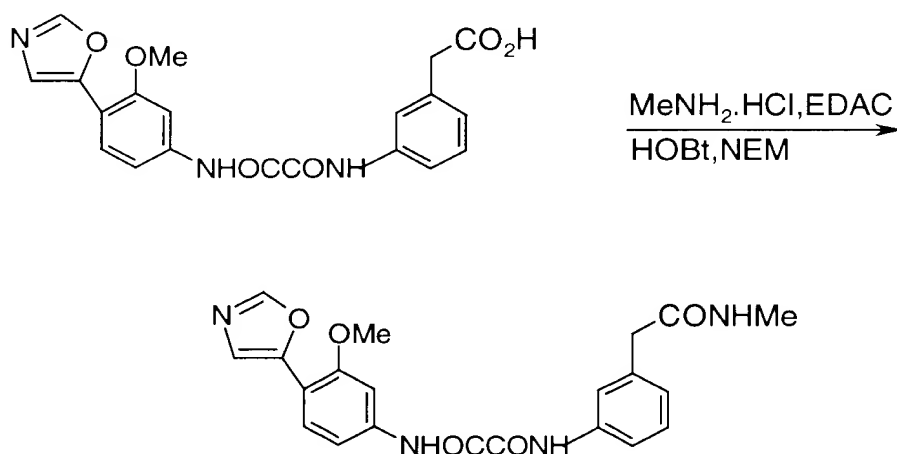


A solution of 30 mg (0.076 mmol) of 2-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]phenyl]acetic acid and 11 mg (0.096 mmol) of N-ethylmorpholine in 1 ml of dimethylformamide was cooled to 0°C and a solution of 12 mg (0.088 mmol) of isobutyl chloroformate in 1 ml of dichloromethane was added. The resulting mixture was stirred for 30 minutes at 0°C then a solution of 7 mg (0.075 mmol) of aniline in 1 ml of dichloromethane was added and stirring was continued for a further hour at 0°C . After 18 hours at room temperature the mixture was evaporated to dryness and the residue chromatographed on silica gel using dichloromethane/methanol (19:1) for the elution. There was obtained 3 mg of N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[3-[(phenylcarbamoyl)methyl]phenyl]oxalamide as a white solid MS: m/e 471.0 $[\text{M}+\text{H}]^+$.

Example 17

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[3-[(methylcarbamoyl)methyl]phenyl]oxalamide

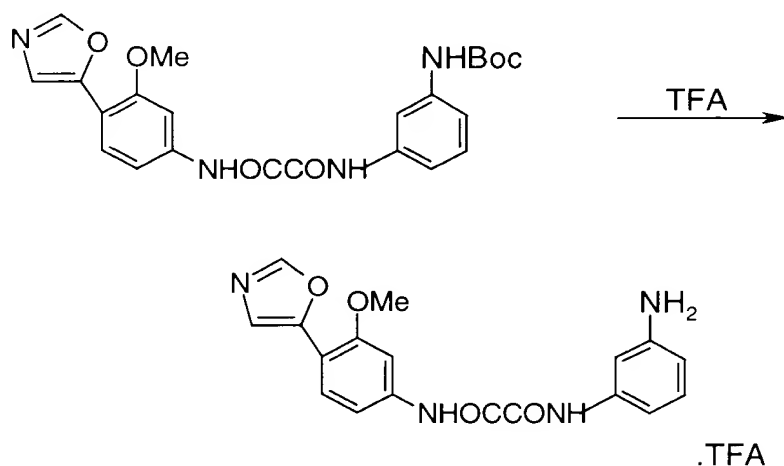
5



A mixture of 30 mg (0.076 mmol) of 2-[3-[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]phenylacetic acid, 22 mg (0.115 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride, 14 mg (0.092 mmol) of 1-hydroxybenzotriazole hydrate, 26 mg (0.385 mmol) of methylamine hydrochloride and 52 mg (0.452 mmol) of N-ethylmorpholine in 1 ml of dimethylformamide was stirred at room temperature for 18 hours. The solvent was removed by evaporation and the residue chromatographed on silica gel using dichloromethane/methanol (1:19) for the elution. There was obtained 15 mg of N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[3-[(methyl carbamoyl)methyl]phenyl]oxalamide as a white solid. MS: m/e 409 [M+H]⁺.

Example 18

N-(3-Aminophenyl)-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide trifluoroacetate

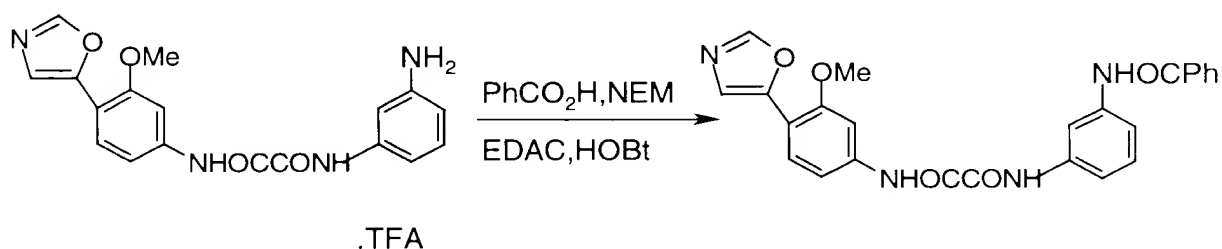


5

20 mg (0.043 mmol) of tert-butyl [3-[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]phenyl]carbamate were dissolved in a mixture of 1 ml of dichloromethane and 1 ml of trifluoroacetic acid at room temperature for 10 minutes. The solvent was removed by evaporation and the residue triturated with diethyl ether. The resulting solid was collected by filtration to give 18 mg of N-(3-aminophenyl)-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide trifluoroacetate as a white solid. MS: m/e 394.0 [M+H+MeCN]⁺.

15 Example 19

N-[3-(Benzamido)phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide

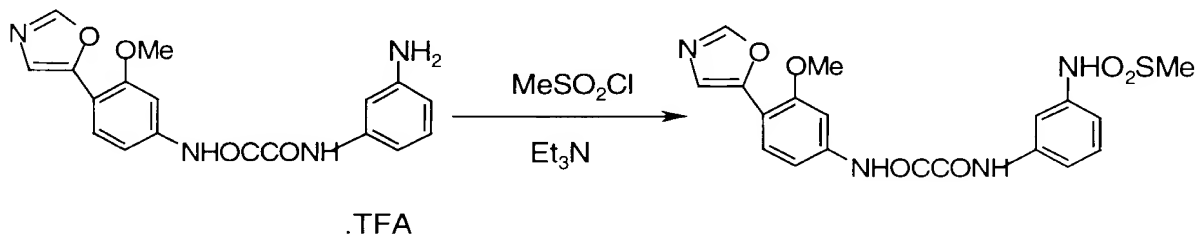


20

A mixture of 30 mg (0.064 mmol) of N-(3-aminophenyl)-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide trifluoroacetate, 9 mg (0.074 mmol) of benzoic acid, 15 mg (0.078 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride, 15 mg (0.096 mmol) of 1-hydroxybenzotriazole hydrate and 22 mg (0.19 mmol) of N-ethylmorpholine in 0.5 ml of dimethylformamide was stirred at room temperature for 18 hours then diluted with ethyl acetate and washed with 10% citric acid solution, saturated sodium bicarbonate and water. The organic phase was dried over magnesium sulphate, evaporated to dryness and the residue chromatographed on silica gel using dichloromethane/methanol (19:1) for the elution. There was obtained after trituration with diethyl ether/petrol (1:1). 12 mg of N-[3-(benzamidophenyl)-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide as a white solid. MS: m/e 457.0 [M+H]⁺.

Example 20

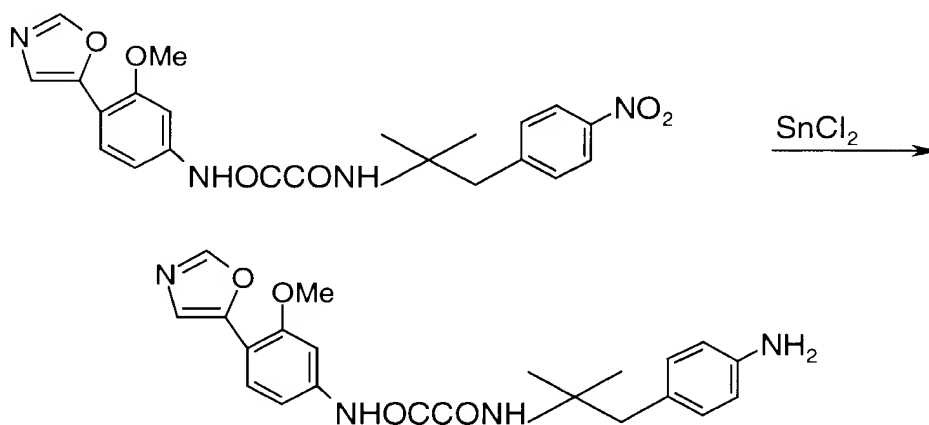
N-[3-(Methanesulphonamido)phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide



12 mg (0.011 mmol) of methanesulphonyl chloride were added to a solution of 50 mg (0.011 mmol) of N-(3-aminophenyl)-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide trifluoroacetate and 32 mg (0.317 mmol) of triethylamine in 0.5 ml of dimethylformamide. The resulting solution was left at room temperature for 18 hours then diluted with ethyl acetate and washed with 10% citric acid solution, saturated sodium bicarbonate and water. The organic phase was dried over magnesium sulphate, evaporated to dryness and the residue chromatographed on silica gel using ethyl acetate/petrol (1:1) for the elution. There was obtained 5 mg of N-[3-(methanesulphonamido)phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide as a white solid. MS: m/e 431.0 [M+H]⁺.

Example 21

N-[2-(4-Aminophenyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide



5

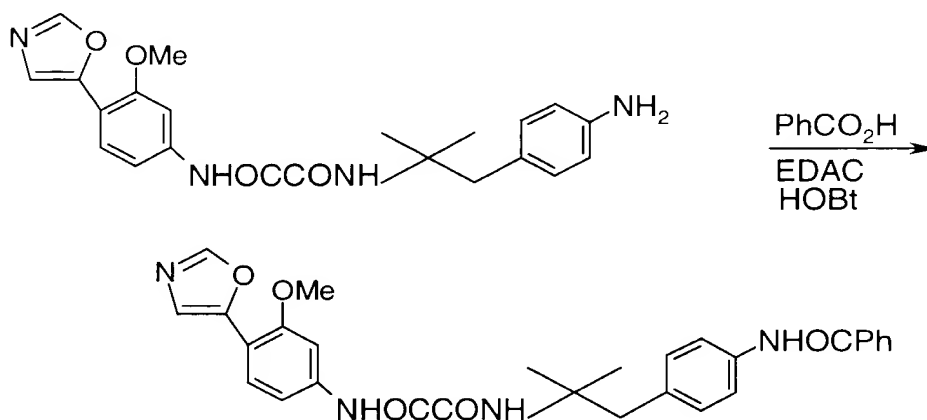
A mixture of 44 mg (0.1 mmol) of N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(4-nitrophenyl)ethyl]oxalamide and 90 mg (0.5 mmol) of tin(II) chloride were stirred and heated at 85°C in 2 ml of ethanol and 1 ml of 1,4-dioxane for 5 hours. The resulting solution was cooled, diluted with ethyl acetate and washed with 2M sodium hydroxide. The organic phase was dried over magnesium sulphate, evaporated to dryness and the residue chromatographed on silica gel using ethyl acetate/petrol (2:1) for the elution. After trituration with petrol there was obtained 31mg of N-[2-(4-aminophenyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide as a white solid. MS: m/e 409 [M+H]⁺.

15

Example 22

N-[2-(4-Benzamidophenyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]
oxalamide

5



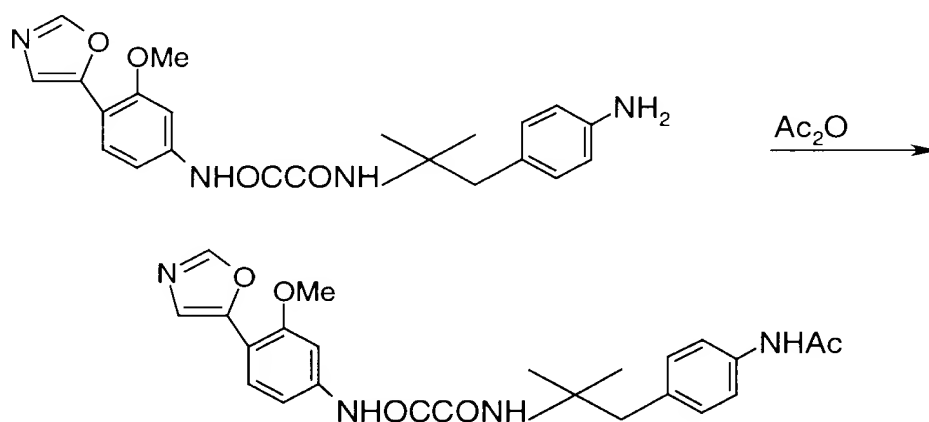
10 A mixture of 30 mg (0.074 mmol) of N-[2-(4-aminophenyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide, 10 mg (0.082 mmol) of benzoic acid, 14 mg (0.092 mmol) of 1-hydroxybenzotriazole hydrate, 21 mg (0.11 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride and 18 mg (0.16 mmol) of N-ethylmorpholine in 2 ml of dichloromethane was stirred at room temperature for 18 hours then diluted with dichloromethane and washed with 2M hydrochloric acid and saturated
15 sodium bicarbonate. The organic phase was dried over magnesium sulphate, evaporated to dryness and the residue chromatographed on silica gel using ethyl acetate/petrol (2:1) for the elution. There was obtained 9 mg of N-[2-(4-benzamidophenyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide as a white solid. MS: m/e 513 [M+H]⁺.

20

Example 23

N-[2-(4-Acetamidophenyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl] oxalamide

5



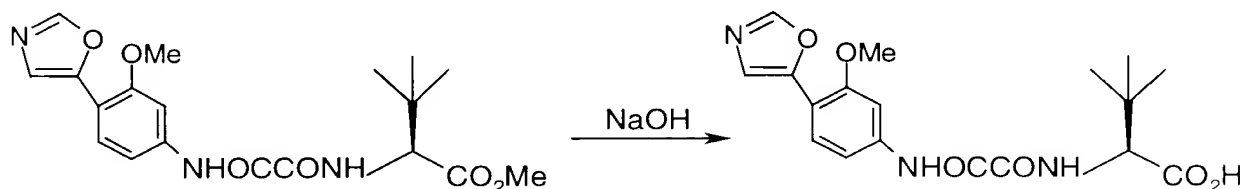
A mixture of 30 mg (0.074 mmol) of N-[2-(4-aminophenyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide, 8 mg (0.078 mmol) of acetic anhydride and 17 mg (0.15 mmol) of N-ethylmorpholine in 1 ml of dichloromethane was stirred at room temperature for 2 hours. The solvent was removed by evaporation and the residue triturated with diethyl ether and collected by filtration to give 14 mg of N-[2-(4-acetamidophenyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide as a white solid. MS: m/e 451 $[M+H]^+$.

15

Example 24

N2-[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]-N1,3-dimethyl-L-valinamide

20

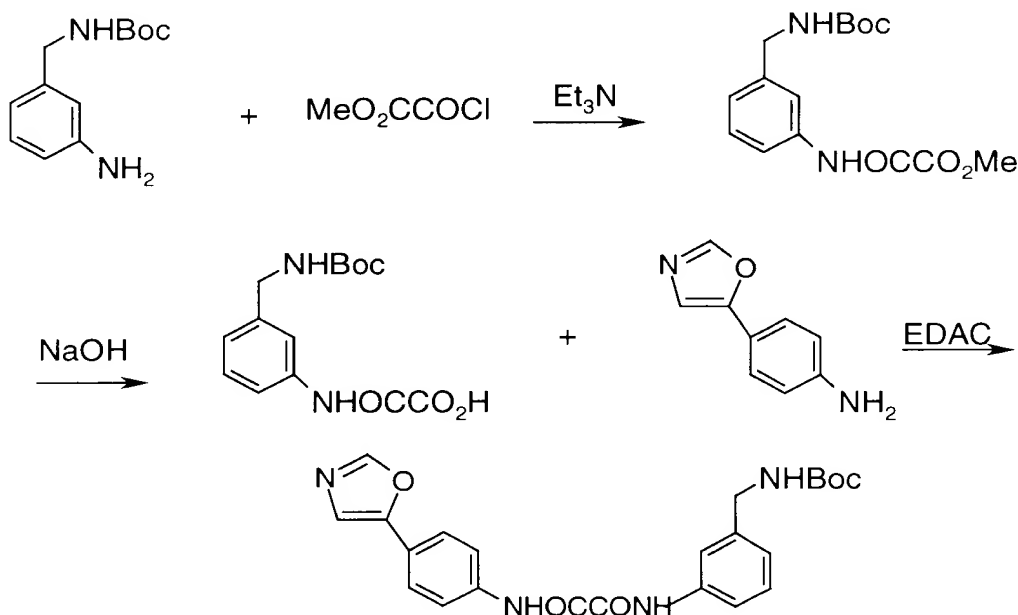


290 mg (0.75 mmol) of N-[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]-3-methyl-L-valine methyl ester in 3 ml of methanol and 1 ml of 1M aqueous sodium hydroxide were warmed gently and the resulting solution left at room temperature for 18 hours. The mixture was
 5 diluted with water, washed with diethyl ether and the aqueous phase acidified with 2M hydrochloric acid. The solution was extracted with ethyl acetate and the organic phase dried over magnesium sulphate, evaporated to dryness and the residue chromatographed on silica gel using ethyl acetate/acetic acid (99:1) for the elution. After trituration with diethyl ether there was obtained 110 mg of N2-[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]-N1,3-dimethyl-
 10 L-valinamide as a white solid. MS: m/e 376.0 [M+H]⁺.

Example 25

Tert-butyl [3-[[[4-(5-oxazolyl)anilino]oxalyl]amino]benzyl]carbamate

15



In an analogous manner to that described in Example 1 but replacing 3-methoxy-4-(5-oxazolyl)aniline with 4-(5-oxazolyl)aniline and N-tert-butyloxalamic acid with N-[3-[(tert-butoxyformamido)methyl]phenyl]oxamic acid there was obtained tert-butyl [3-[[[4-(5-oxazolyl)anilino] oxalyl]amino]benzyl]carbamate as a white solid. ¹H NMR (400 MHz,
 20

DMSO) δ : 1.4 (9H,s), 4.1 (2H,d), 7.02 (1H,d), 7.32 (1H,t), 7.40 (1H,t), 7.63 (1H,s), 7.69 (1H,d), 7.70-7.79 (3H,m), 7.97 (2H,d), 8.43 (1H,s), 10.82 (1H,s), 10.99 (1H,s).

The starting material was prepared as follows:

5

i) 586 mg (4.78 mmol) of methyl oxalyl chloride were added to a solution of 1 g (4.5 mmol) of *tert*-butyl (3-aminobenzyl)carbamate and 508 mg (5.03 mmol) of triethylamine in 10 ml of dichloromethane. The resulting solution was stirred at room temperature for 30 minutes then washed with 5% citric acid solution and saturated sodium bicarbonate. The organic phase was dried over magnesium sulphate and the solvent removed by evaporation to give 1.5 g of methyl N-[3-[(*tert*-butoxyformamido)methyl]phenyl]oxamate as a viscous gum. ^1H NMR (400 MHz, CDCl_3) δ : 1.43 (9H,s), 3.96 (3H,s), 4.31 (2H,d), 4.9-5.0 (br.s, 1H), 7.11 (1H,d), 7.33 (1H,t), 7.51 (1H,s), 7.52 (1H,d), 8.86 (br.s, 1H).

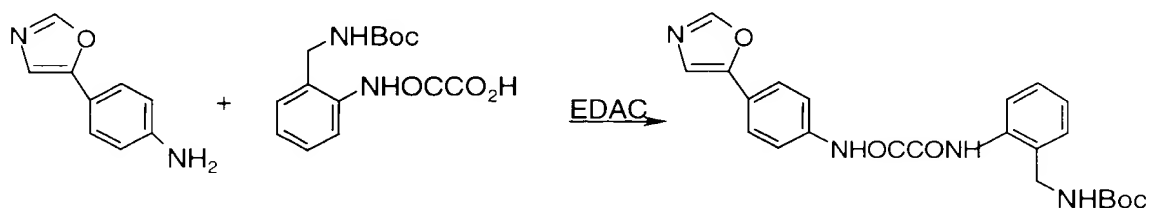
15

ii) A mixture of 1.232 g (4 mmol) of methyl N-[3-[(*tert*-butoxy formamido)methyl]phenyl]oxamate and 0.24 g (6 mmol) of sodium hydroxide in 15 ml of methanol/water (2:1) was stirred at room temperature for 2 hours. The solvent was removed by evaporation and the residue dissolved in water and diethyl ether. The aqueous layer was acidified with citric acid and washed twice with ethyl acetate. The combined organic solutions were dried over magnesium sulphate and the solvent removed by evaporation to give 670 mg of N-[3-[(*tert*-butoxyformamido)methyl]phenyl]oxamic acid as a white solid. ^1H NMR (400 MHz, DMSO) δ : 1.48 (9H,s), 4.17 (2H,d), 7.09 (1H,d), 7.36 (1H,t), 7.49 (1H, t), 7.64 (1H,d), 7.74 (1H,s), 10.75 (1H,s).

25

Example 26

Tert-butyl [2-[[[4-(5-oxazolyl)anilino]oxalyl]amino]benzyl]carbamate

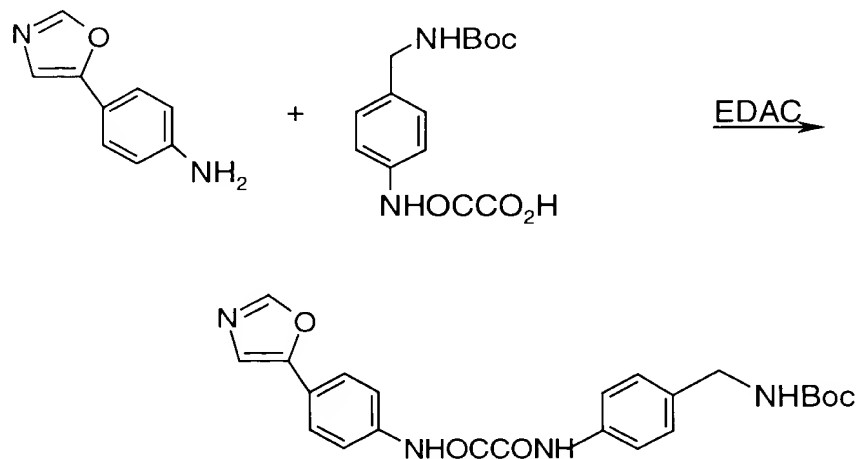


In an analogous manner to that described in Example 25 but replacing N-[3-[(tert-butoxyformamido)methyl]phenyl]oxamic acid with N-[2-[(tert-butoxyformamido)methyl]phenyl]oxamic acid there was obtained tert-butyl [2-[[[4-(5-oxazolyl)anilino]oxalyl]amino]benzyl]carbamate as a white solid MS: m/e 437.0 [M+H]⁺.

10

Example 27

Tert-butyl [4-[[[4-(5-oxazolyl)anilino]oxalyl]amino]benzyl]carbamate



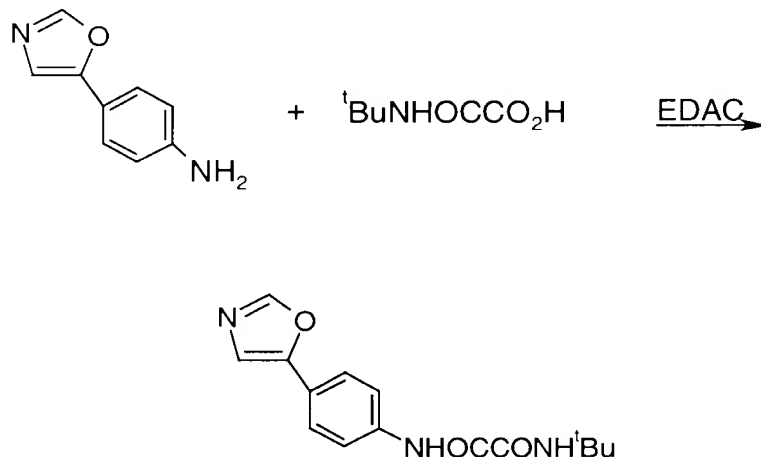
15

In an analogous manner to that described in Example 25 but replacing N-[3-[(tert-butoxyformamido)methyl]phenyl]oxamic acid with N-[4-[(tert-butoxyformamido)methyl]phenyl]oxamic acid there was obtained tert-butyl [4-[[[4-(5-oxazolyl)anilino]oxalyl]amino]benzyl]carbamate as a white solid. MS: m/e 436.6 [M]⁺.

20

Example 28

N-Tert-butyl-N'-[4-(5-oxazolyl)phenyl]oxalamide

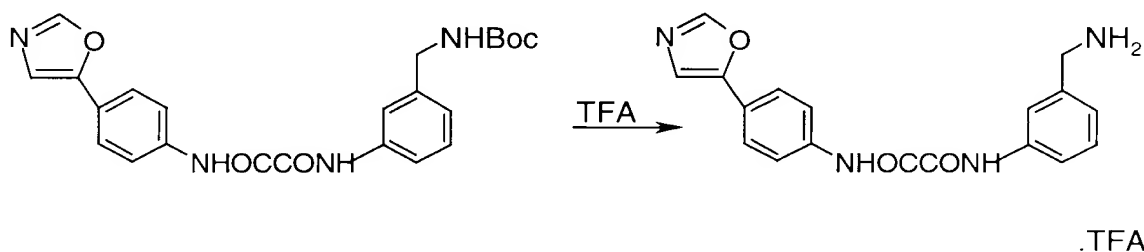


5

In an analogous manner to that described in Example 1 but replacing 3-methoxy-4-(5-oxazolyl)aniline with 4-(5-oxazolyl)aniline there was obtained N-tert-butyl-N'-[4-(5-oxazolyl)phenyl]oxalamide as a pale yellow solid. MS: m/e 329.0 $[\text{M}+\text{H}+\text{MeCN}]^+$.

10 Example 29

N-[3-(Aminomethyl)phenyl]-N'-[4-(5-oxazolyl)phenyl]oxalamide trifluoroacetate



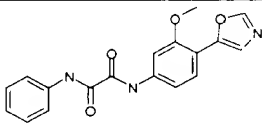
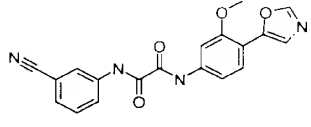
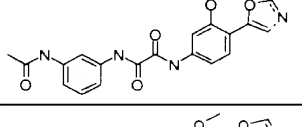
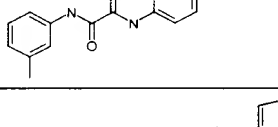
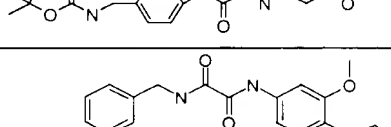
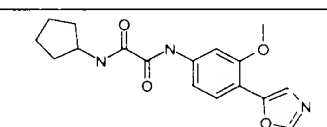
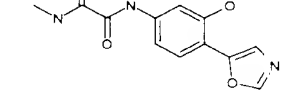
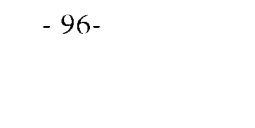
15

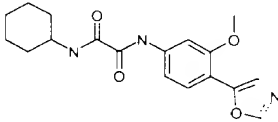
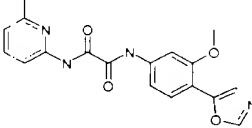
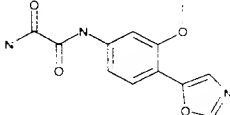
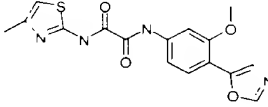
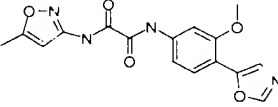
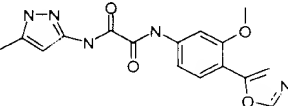
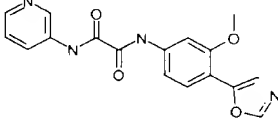
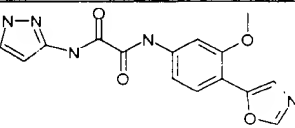
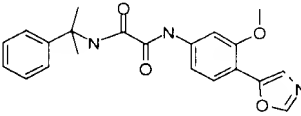
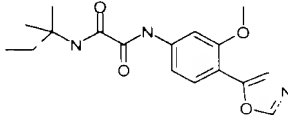
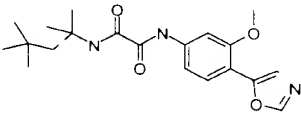
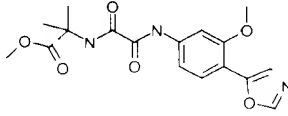
In an analogous manner to that described in Example 3 but replacing tert-butyl [3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]benzyl]carbamate with tert-butyl [3-[[[4-(5-oxazolyl)oxalyl]amino]benzyl]carbamate there was obtained N-[3-(aminomethyl)phenyl]-N'-[4-(5-oxazolyl)phenyl]oxalamide trifluoroacetate as a white solid. MS: m/e 336 $[\text{M}]^+$.

Examples 30-193

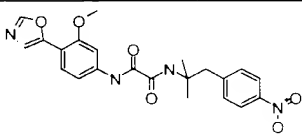
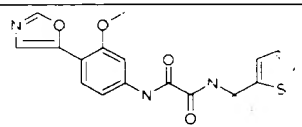
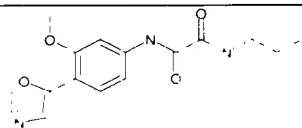
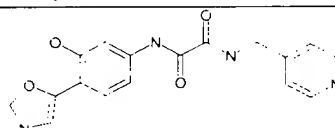
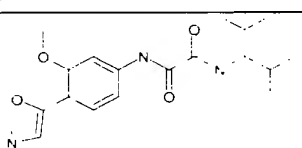
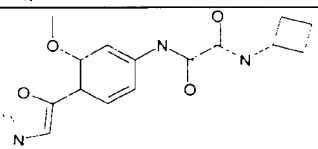
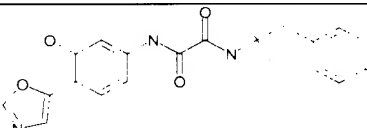
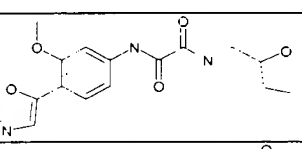
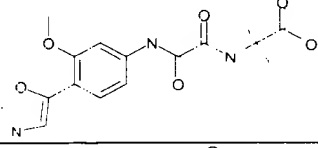
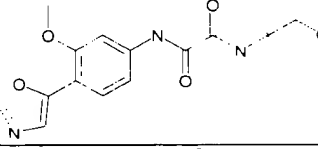
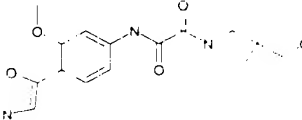
In a manner analogous to that described in Example 1, starting with N-[3-methoxy-4-(5-oxazolyl)phenyl oxalamic acid (prepared as described in Example 1, parts (i) and (ii)) and the appropriate amine the compounds shown in Table 3 were also prepared:

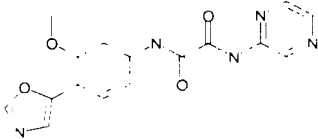
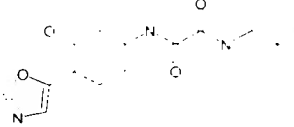
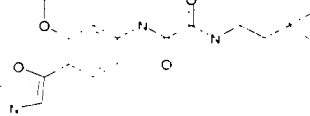
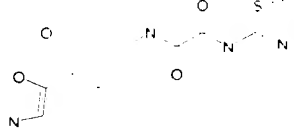
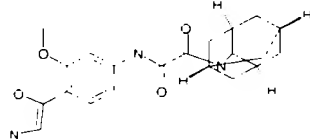
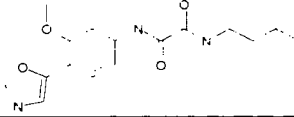
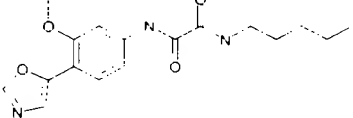
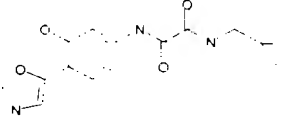
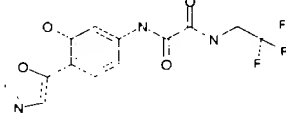
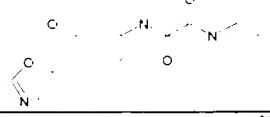
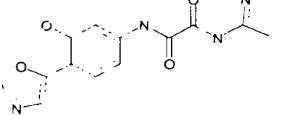
Table 3

Example	Structure	MS(ES)
30.		338.0
31.		362.9
32.		395.0
33.		352.0
34.		466 (M ⁺ ;EI)
35.		352.0
36.		330.0
37.		275.9

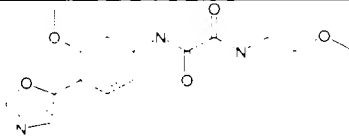
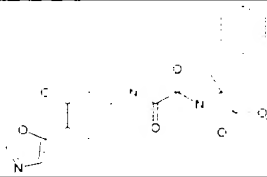
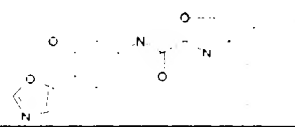
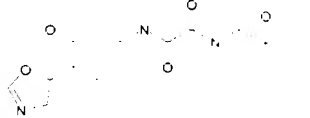
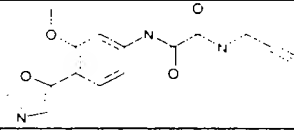
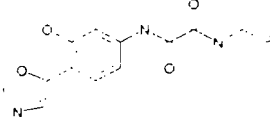
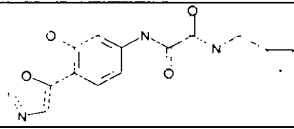
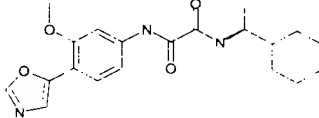
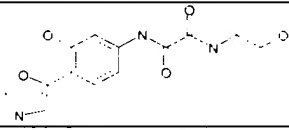
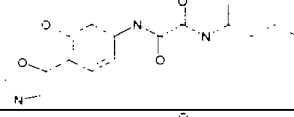
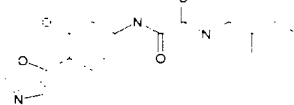
38.		344.0
39.		352.9
40.		261.9
41.		358.9
42.		342.9
43.		341.9
44.		338.9
45.		327.9
46.		380.0
47.		332.0
48.		374.0
49.		362.0

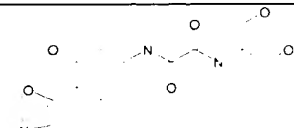
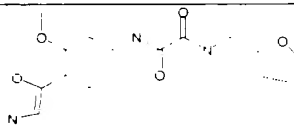
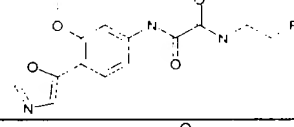
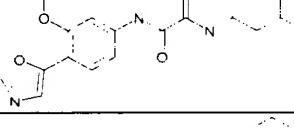
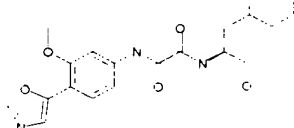
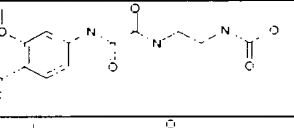
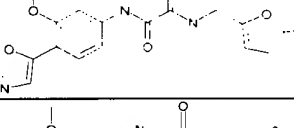
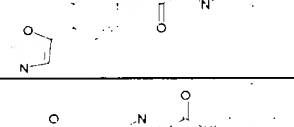
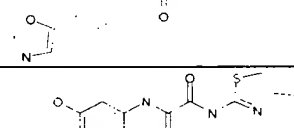
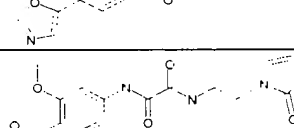
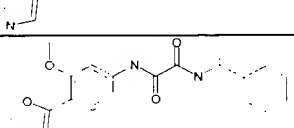
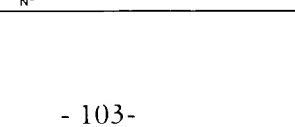
50.		317.9
51.		332.0
52.		361.0
53.		389.9
54.		328.0
55.		346.0
56.		289.9
57.		318.0
58.		304.0
59.		333.9
60.		394.0

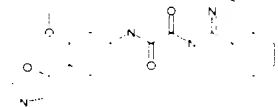
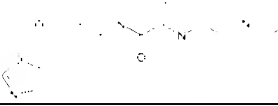
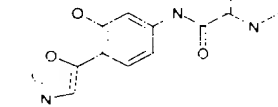
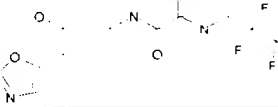
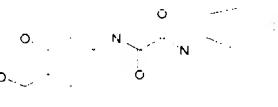
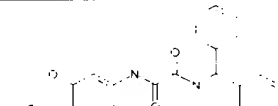
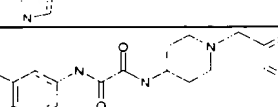
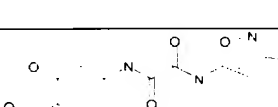
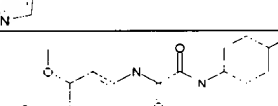
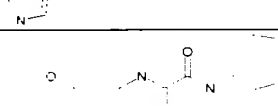
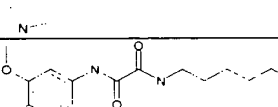
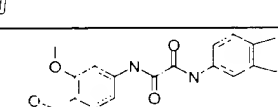
61.		439 (M ⁺ ;EI)
62.		386 (M ⁺ ;EI)
63.		304.0
64.		353.2
65.		360.2
66.		316.2
67.		412.2
68.		345.8
69.		362.4
70.		334.2
71.		348.0

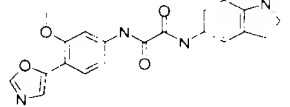
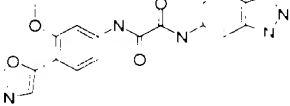
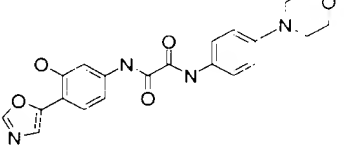
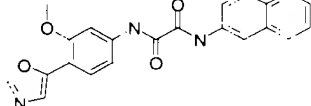
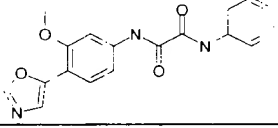
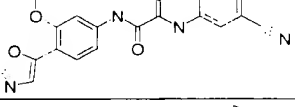
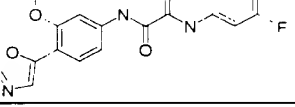
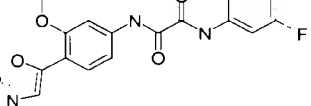
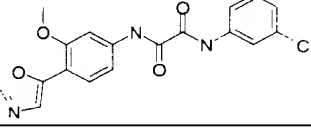
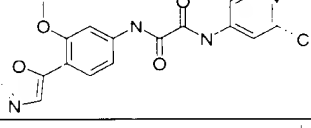
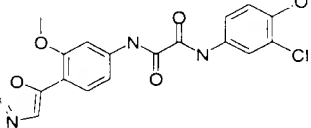
72.		340.0
73.		345.8
74.		346.0
75.		346.8
76.		395.8
77.		332.4
78.		332.4
79.		316.2
80.		344.0
81.		317.8
82.		328.2

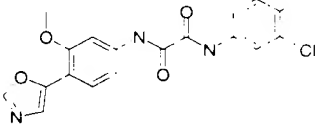
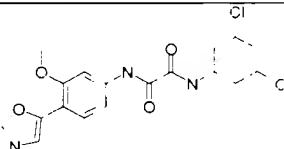
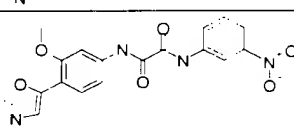
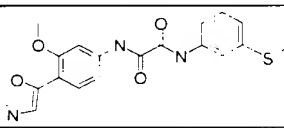
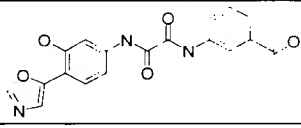
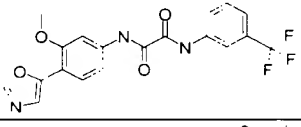
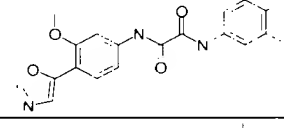
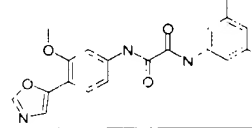
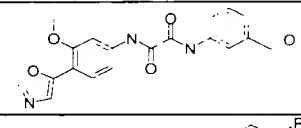
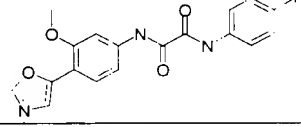
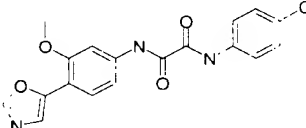
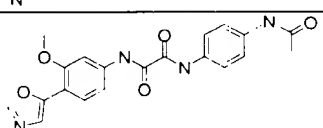
83.		332.4
84.		334.2
85.		334.2
86.		339.2
87.		344.8
88.		348.0
89.		359.2
90.		358.2
91.		366.2
92.		389.4
93.		306.2

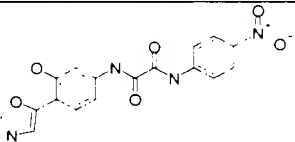
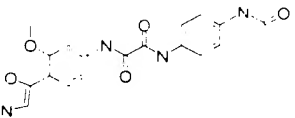
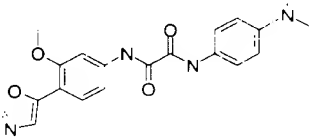
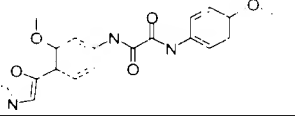
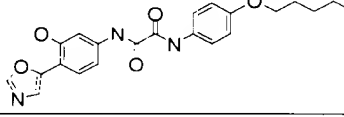
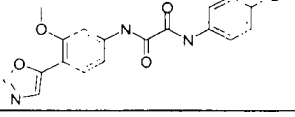
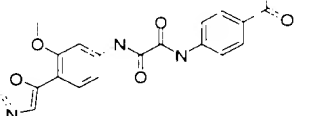
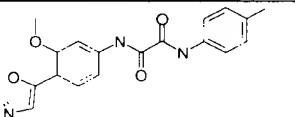
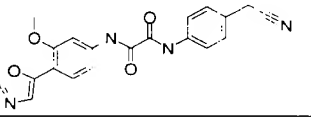
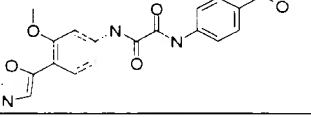
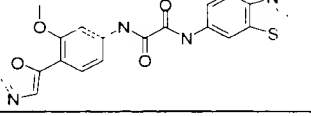
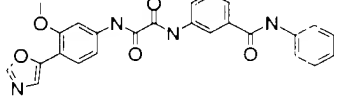
94.		319.8
95.		438.0
96.		504.2
97.		374.0
98.		299.8
99.		302.2
100.		316.2
101.		372.0
102.		319.8
103.		332.4
104.		332.4

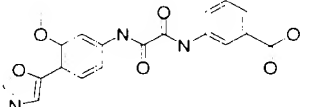
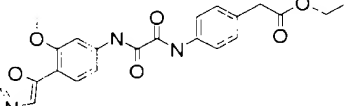
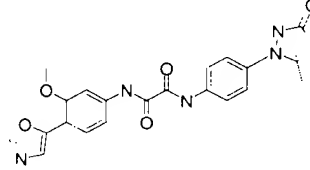
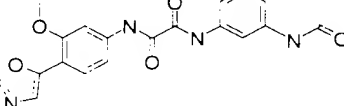
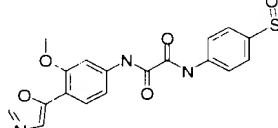
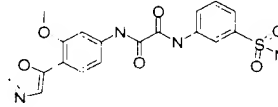
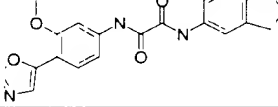
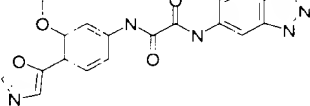
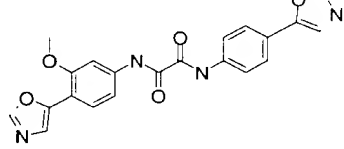
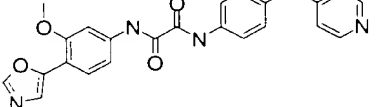
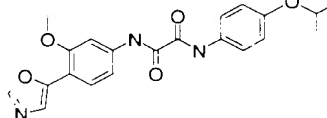
105.		336.6
106.		342.0
107.		308.0
108.		345.8
109.		402.0
110.		405.2
111.		356.0
112.		358.2
113.		358.2
114.		359.2
115.		374.0
116.		372.0

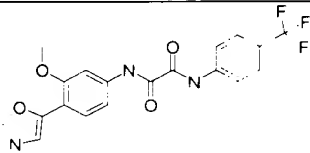
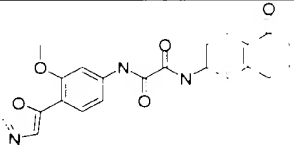
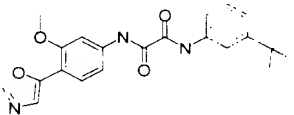
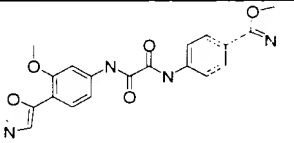
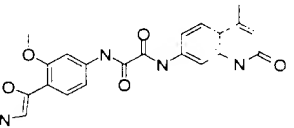
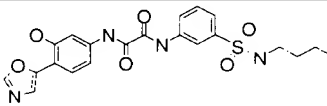
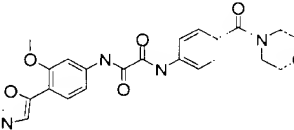
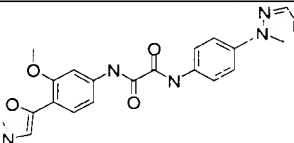
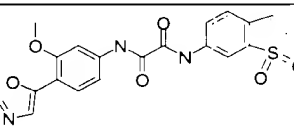
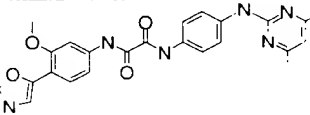
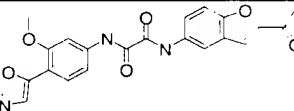
117.		389.2
118.		389.4
119.		276.0
120.		394 (M ⁺ ;EI)
121.		378.4
122.		428 (M ⁺ ;EI)
123.		435.2
124.		357.2
125.		358.2
126.		358.2
127.		360.2
128.		378.4

129.		377.4
130.		378.4
131.		423
132.		389.4
133.		338.2
134.		363.4
135.		356
136.		370
137.		371.8
138.		406.2
139.		402.2

140.		386.2
141.		406.2
142.		383.2
143.		384
144.		380.2
145.		406.2
146.		366.2
147.		366.2
148.		368.2
149.		356
150.		371.8
151.		395

152.		383.2
153.		409.4
154.		380.8
155.		368.2
156.		424.2
157.		354.2
158.		380.2
159.		352.4
160.		377.4
161.		368.2
162.		395
163.		457.4

164.		396
165.		424
166.		434.2
167.		395
168.		416.4
169.		417.4
170.		378.4
171.		379.2
172.		405.2
173.		428.8
174.		396

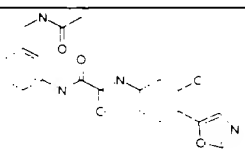
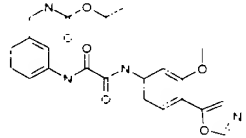
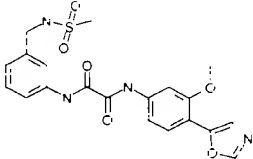
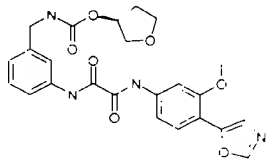
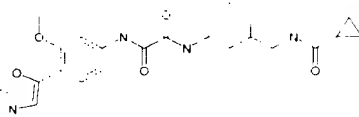
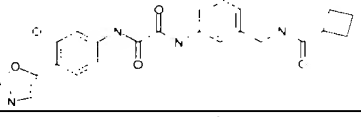
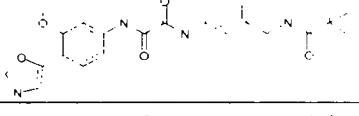
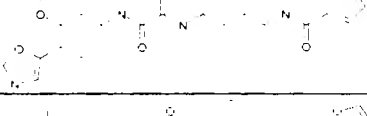
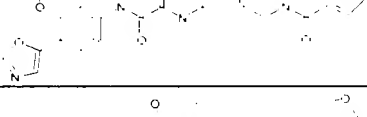
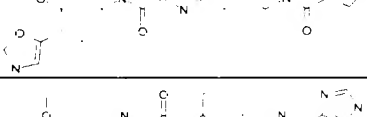

175.		406.2
176.		406.2
177.		394.2
178.		407
179.		507.2
180.		473.2
181.		451.2
182.		405.2
183.		426
184.		459.2
185.		420.2

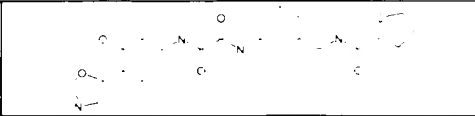
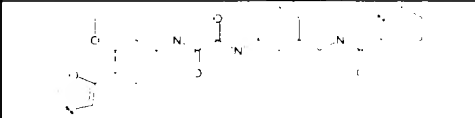
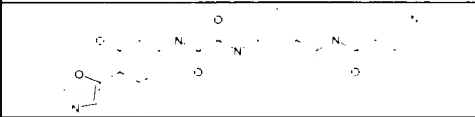
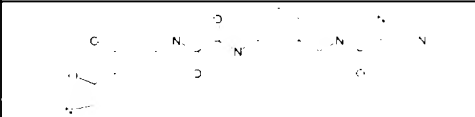
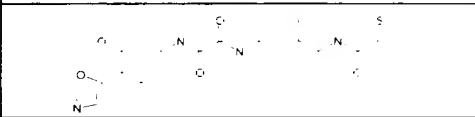
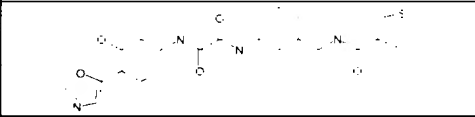
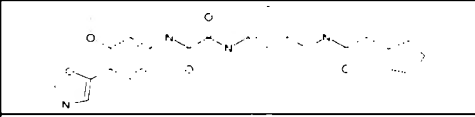
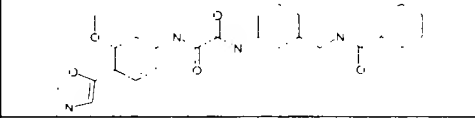
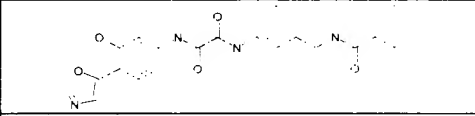
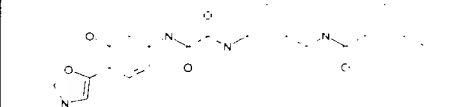
186.		409.4
187.		485.4
188.		471.6
189.		487.2
190.		437.2
191.		409.4
192.		445.2
193.		464

Examples 194- 214

5 In a manner analogous to that described in Example 4, starting with N-[3-(aminomethyl)phenyl]-N'-[3-methoxy-4-(5-(oxazolyl)phenyl)]oxalamide trifluoroacetate (prepared as described in Example 3) and the appropriate carboxylic acid derivative the compounds shown in Table 5 also were prepared:

Table 5

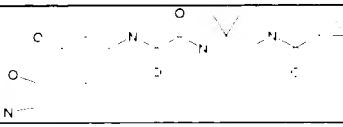
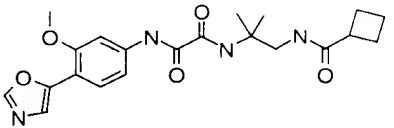
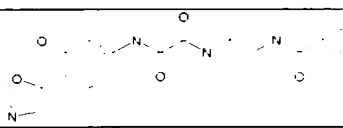
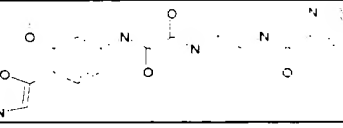
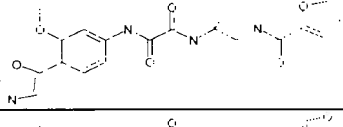
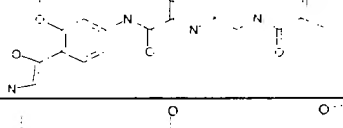
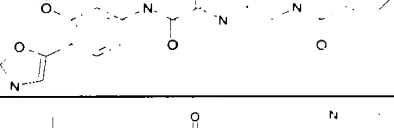
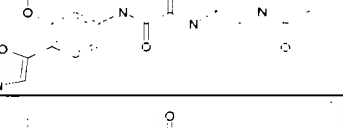
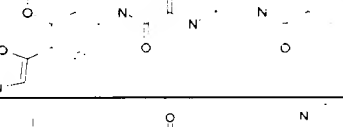
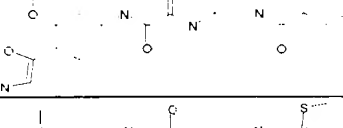
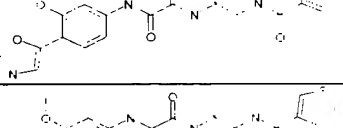
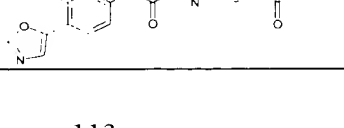
Example	Structure	MS(ES)
194.		409.1
195.		453.0
196.		445.0
197.		481.0
198.		435.1
199.		449.1
200.		451.2
201.		460.0
202.		461.1
203.		461.0
204.		461.0

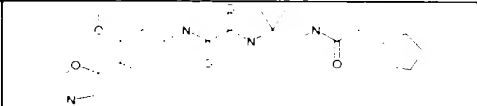
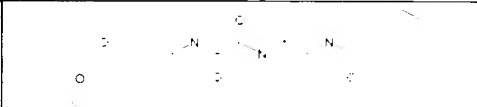
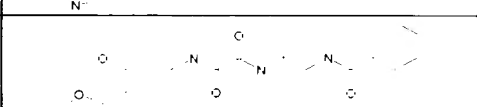
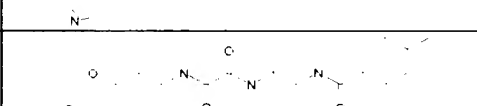
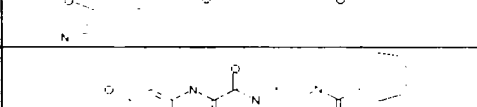
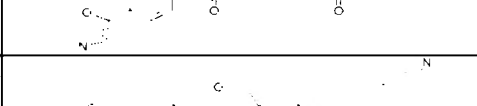
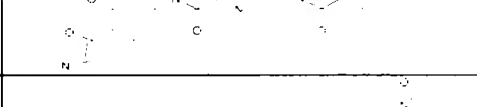

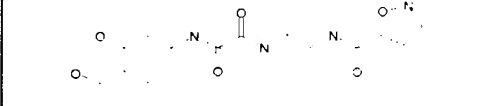
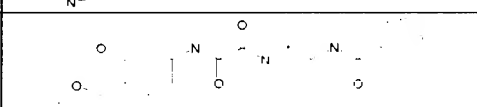
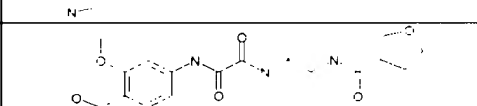
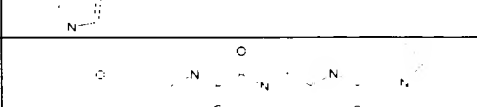
205.		465.1
206.		472.1
207.		472.0
208.		473.0
209.		477.0
210.		477.0
211.		477.2
212.		477.2
213.		485.1
214.		485.2

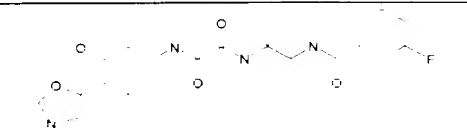
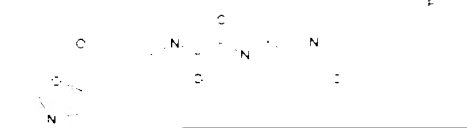
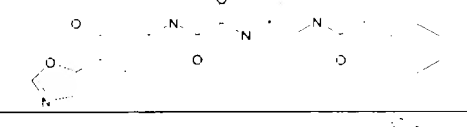
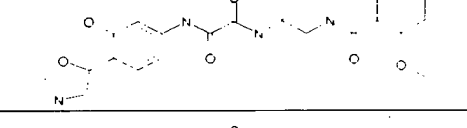
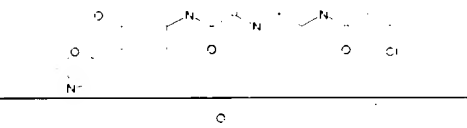
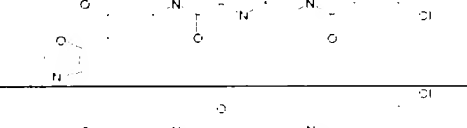
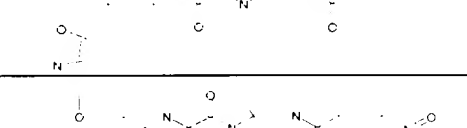
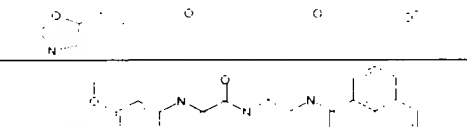
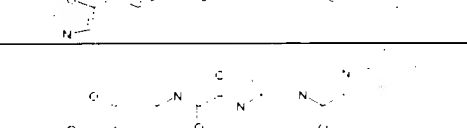
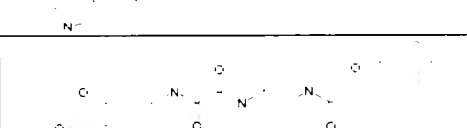
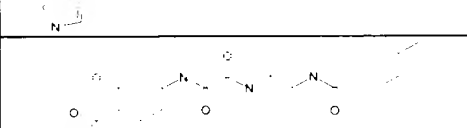
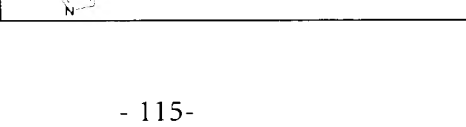
Examples 215 - 301

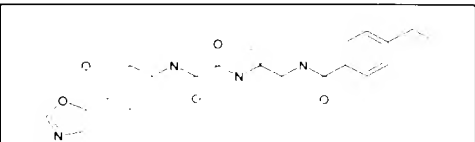
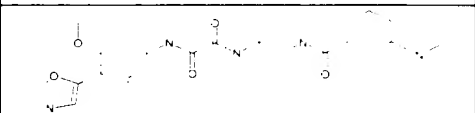
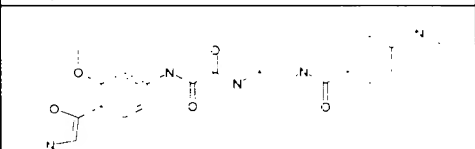
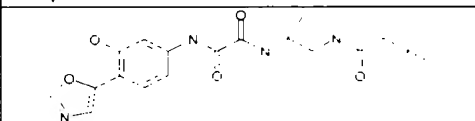
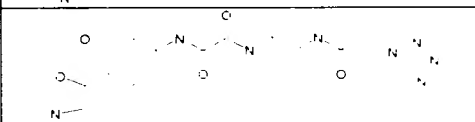
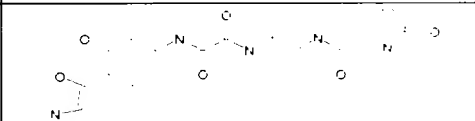
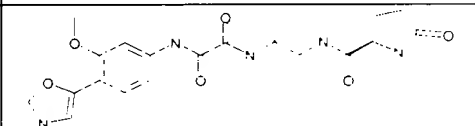
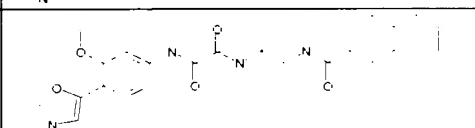
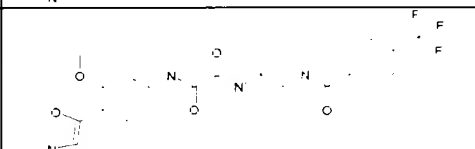
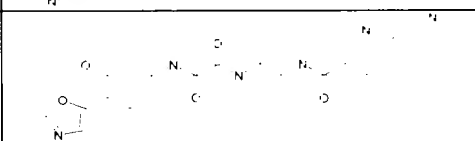
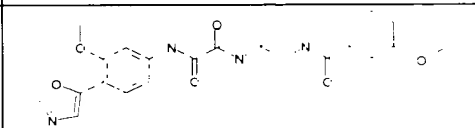
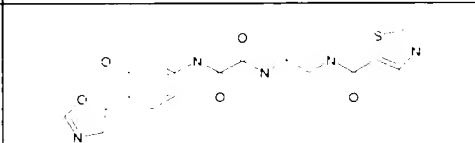
In a manner analogous to that described in Example 10, starting with N-[2-amino-1,1-dimethylethyl)-N'-(3-methoxy-4-oxazol-5-ylphenyl)oxalamide (prepared as described in Example 9) and the appropriate carboxylic acid the compounds shown in table 4 were also prepared:

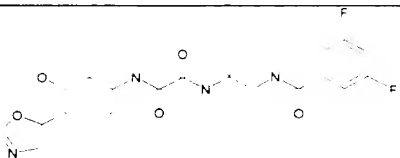
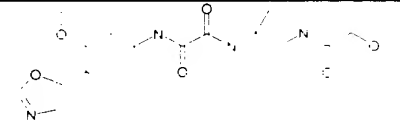
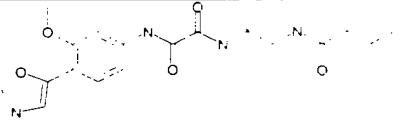
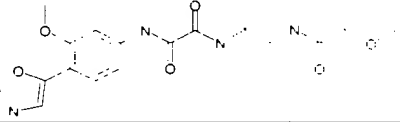
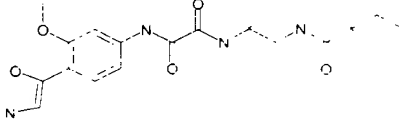
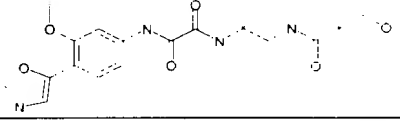
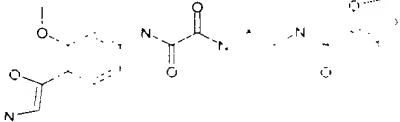
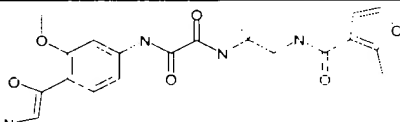
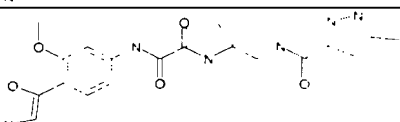
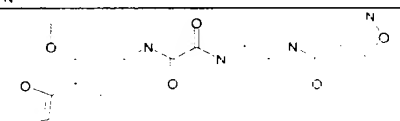
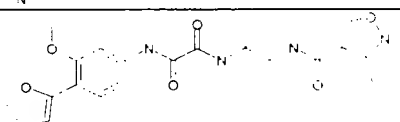
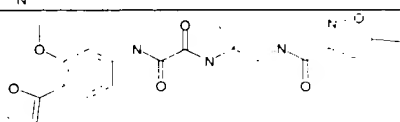
Table 4

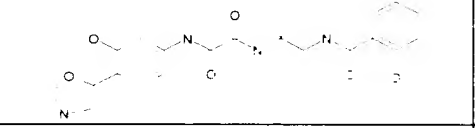
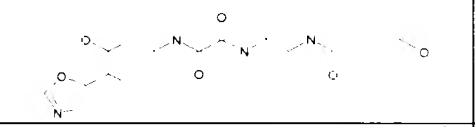
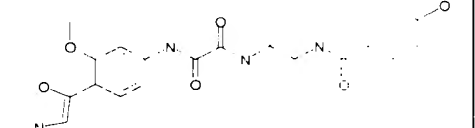
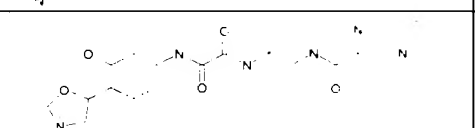
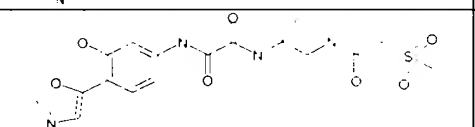
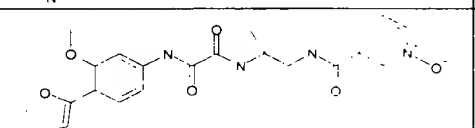
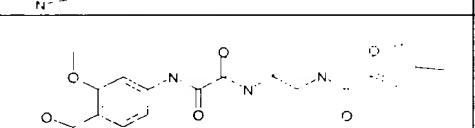
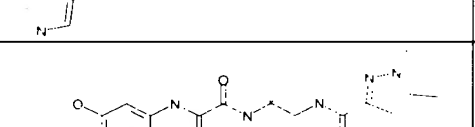
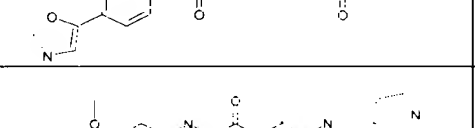
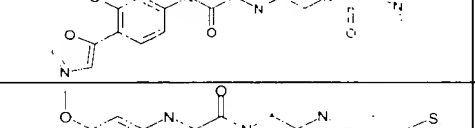
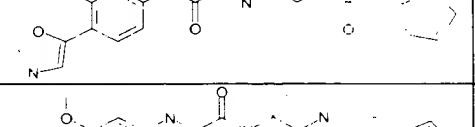
Example	Structure	MS(ES)
215.		401.0
216.		415.0
217.		417.0
218.		426.0
219.		427.0
220.		427.0
221.		431.0
222.		438.0
223.		438.0
224.		439.0
225.		443.0
226.		443.0

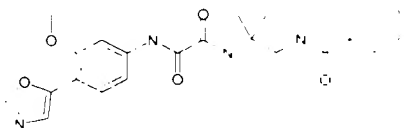

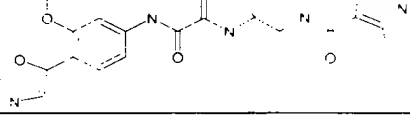
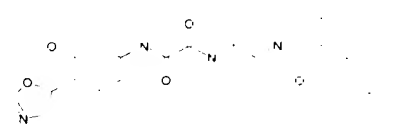
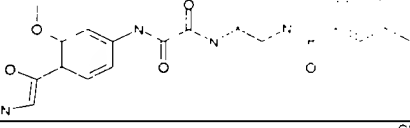
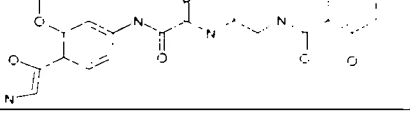
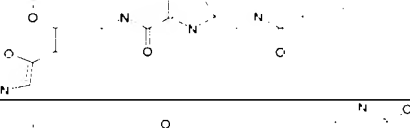
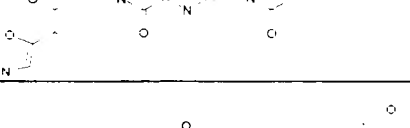
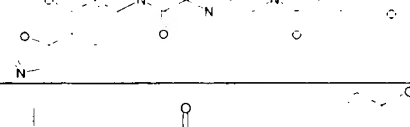
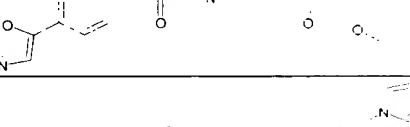
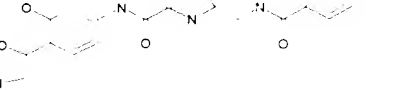
227.		443.1
228.		443.1
229.		451.0
230.		451.0
231.		457.1
232.		462.0
233.		482.0
234.		428.0
235.		429.1
236.		431.0
237.		440.0
238.		445.0

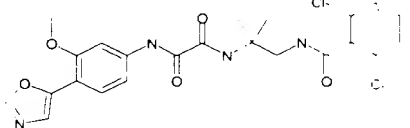
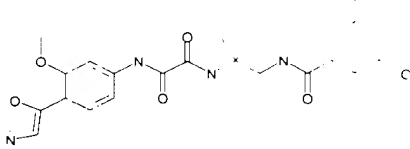
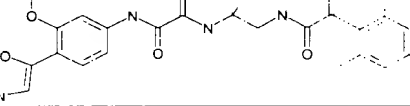
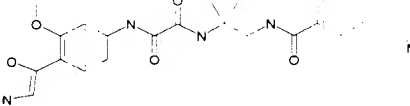
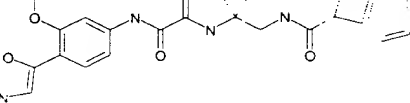
239.		455.0
240.		455.0
241.		457.1
242.		467.1
243.		471.0
244.		471.0
245.		471.0
246.		482.0
247.		487.1
248.		476.1
249.		477.1
250.		479.1

251.		479.1
252.		480.1
253.		480.1
254.		431.1
255.		443.0
256.		444.0
257.		444.0
258.		487.1
259.		505.1
260.		463.0
261.		467.1
262.		472.0

263.		473.0
264.		391.0
265.		401.0
266.		405.0
267.		431.1
268.		433.0
269.		441.0
270.		441.0
271.		441.0
272.		442.0
273.		442.0
274.		442.0

275.		453.0
276.		453.0
277.		453.0
278.		453.0
279.		453.0
280.		454.0
281.		455.0
282.		455.0
283.		455.0
284.		457.0
285.		457.0

286.		457.1
287.		457.1
288.		459.0
289.		527.2
290.		563.0
291.		487.0
292.		494.1
293.		494.1
294.		497.1
295.		501.0
296.		502.1

297.		505.0
298.		505.0
299.		507.1
300.		462.0
301.		463.1

Examples 302-315 ; 438-458 and 653-663

Typical methods used for the preparation of compounds of table 1c are described
5 below:

Example 440

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(1-oxido-4-pyridyl)ethyl]oxalamide

10

30 mg (0.1 mmol) of 60% 3-chloroperoxybenzoic acid were added to a stirred solution of 20 mg (0.051 mmol) of N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(4-pyridyl)ethyl]oxalamide in 1 ml of dichloromethane. The mixture was stirred for 1 hour then diluted with ethyl acetate, washed with sodium bisulphite solution, sodium bicarbonate
15 solution and brine. The organic solution was dried over magnesium sulphate, evaporated to dryness and the residue triturated with diethyl ether to give 13 mg of N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(1-oxido-4-pyridyl)ethyl]oxalamide as an off-white solid. MS: m/e 411 [M+H]⁺.

The starting material was prepared as follows:

- i) A solution of 17.4 g (0.115 mol) of alpha, alpha-dimethyl-4-pyridineethanol in 115 ml of acetic acid was added dropwise to a mixture of 115 ml of acetic acid, 58 ml of concentrated sulphuric acid and 6.8 ml (0.126 mmol) of acetonitrile with cooling in an ice/salt bath. The resulting mixture was stirred for 2 hours at room temperature and the pH raised to 10 by the addition of 6M sodium hydroxide solution with ice cooling. The slurry was filtered, washed with ethyl acetate and the aqueous filtrate extracted twice with ethyl acetate. The combined organic extracts were dried over magnesium sulphate, evaporated to dryness and the residue chromatographed on silica gel using ethyl acetate/methanol (1:19), (1:9) and (3:17) for the gradient elution. There was obtained 1.87 g of N-[1,1-dimethyl-2-(4-pyridyl)ethyl]acetamide as an orange oil. ¹H NMR (400 MHz CDCl₃) δ: 1.29 (6H,s), 1.91 (3H,s), 3.11 (2H,s), 5.10 (1H,br.s.), 7.07 (2H,d), 8.50(2H,d).
- ii) A solution of 1.8 g (9.3 mmol) of N-[1,1-dimethyl-2-(4-pyridyl)ethyl]acetamide, 2.66 g (9.3 mmol) of titanium (IV) isopropoxide and 2.56 g (14 mmol) of diphenylsilane in 10 ml of tetrahydrofuran was stirred at room temperature for 20 hours. The resulting mixture was chromatographed on silica gel using dichloromethane/methanol/acetic acid/water (60:18:2:3) for the elution. The product was dissolved in 20 ml of concentrated hydrochloric acid and 50 ml of methanol and evaporated to dryness. The residue was evaporated with toluene five times to give 620 mg of alpha, alpha-dimethyl-4-pyridineethylamine hydrochloride (1:1), as a pale brown solid. ¹H NMR (400 MHz DMSO) δ: 1.31 (6H,s), 3.26 (2H,s), 8.02 (2H,d), 8.4-8.6 (3H,br.s), 8.88 (2H,d).
- iii) A mixture of 100 mg (0.45 mmol) of alpha, alpha-dimethyl-4-pyridineethylamine hydrochloride (1:1), 120 mg (0.45 mmol) of N-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamic acid, 105 mg (0.68 mmol) of 1-hydroxybenzotriazole hydrate, 105 mg (0.54 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride and 127 mg (1.1 mmol) of N-ethylmorpholine in 4 ml of dichloromethane was stirred for 20 hours at room temperature then diluted with ethyl acetate and washed with water and brine. The organic solution was dried over magnesium sulphate, evaporated to dryness and the residue chromatographed on silica gel using ethyl acetate/methanol (19:1) for the elution. After trituration with diethyl ether there was obtained 32 mg of N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(4-

pyridyl)ethyl]oxalamide as a white solid. MS: m/e 395 [M+H]⁺.

Example 455

5 2-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]-5-benzofurancarboxylic acid

10 A solution of 68 mg (0.12 mmol) of benzyl 2-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]-5-benzofurancarboxylate in 10 ml of tetrahydrofuran was hydrogenated with 20 mg of 10% palladium on carbon for 4 hours. The resulting suspension was filtered, evaporated to dryness and the residue triturated with diethyl ether to give 41 mg of 2-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]-5-benzofurancarboxylic acid as a white solid. MS: m/e 477.9 [M+H]⁺.

15 The starting material was prepared as follows:

i) A solution of 1.976 g (22.46 mmol) of isobutyric acid in 8 ml of anhydrous tetrahydrofuran was added to a stirred suspension of 1.078 g (26.95 mmol) of 60% sodium hydride and 2.268 g (22.46 mmol) of diisopropylamine in 40 ml of anhydrous tetrahydrofuran under a nitrogen atmosphere and the mixture heated to reflux for 15 minutes. After cooling to 0°C a solution of 14.04 ml (22.46 mmol) of 1.6M butyllithium in hexanes was added maintaining the temperature at 0-5°C. After 5 minutes at 0°C the mixture was warmed to 30-35°C for 20 minutes, cooled to 0°C and a solution of 5.3 g (22.46 mmol) of 2-(bromomethyl)-5-benzofurancarbonitrile in 15 ml of anhydrous tetrahydrofuran was added maintaining the temperature at 0°C. The suspension was stirred for 5 minutes at 0°C then warmed to 30-35°C for 20 minutes before being cooled to 15°C and quenched by the careful addition of 50 ml of water and diluted with 50 ml of diethyl ether. The aqueous phase was separated, acidified with concentrated hydrochloric acid and extracted with diethyl ether. The organic phase was dried over magnesium sulphate, evaporated to dryness and the residue chromatographed on silica gel using ethyl acetate/petrol (1:2) for the elution. There was obtained 670 mg of 5-cyano- α , α -dimethyl-2-benzofuranpropionic acid as a white

25
30

solid. ^1H NMR (400 MHz CDCl_3) δ : 1.23 (6H,s), 3.01 (2H,s), 6.46 (1H,s), 7.38 (1H,d), 7.42 (1H,d), 7.75 (1H,s).

ii) A mixture of 652 mg (2.68 mmol) of 5-cyano- α , α -dimethyl-2-benzofuranpropionic acid, 732 mg (2.68 mmol) of diphenylphosphoryl azide and 269 mg (2.66 mmol) of triethylamine in 8 ml of tert-butanol was refluxed for 8 hours then evaporated to dryness and the residue dissolved in ethyl acetate and washed with saturated sodium bicarbonate solution. The organic phase was dried over magnesium sulphate, evaporated to dryness and chromatographed on silica gel using ethyl acetate/petrol (2:3) for the elution to give 225 mg of white solid which was suspended in 10 ml of 2M sodium hydroxide solution and stirred and refluxed for 20 hours. The resulting suspension was cooled, evaporated to dryness and 5 ml of ethylene glycol and 400 mg of potassium hydroxide were added. After heating at 190°C for 20 minutes 2 ml of water were added and after a further 20 minutes another 15 ml of water were added and heating continued for 20 minutes until a thick paste remained which was cooled and dissolved in 20 ml of water. Concentrated hydrochloric acid was added to bring the pH to 2 then 25 ml of dioxan, 3 g (21.74 mmol) of potassium carbonate and 1.5 g (6.88 mmol) of di-tert-butyl dicarbonate were added and the mixture stirred for 24 hours. The solvent was removed by evaporation and the residue dissolved in diethyl ether and water. The aqueous phase was separated, acidified with 2M hydrochloric acid and extracted with diethyl ether. The organic phase was dried over magnesium sulphate and evaporated to dryness to give 106 mg of 2-[2-(tert-butoxyformamido)-2-methylpropyl]-5-benzofurancarboxylic acid as a colourless gum.

iii) A mixture of 105 mg (0.32 mmol) of 2-[2-(tert-butoxyformamido)-2-methylpropyl]-5-benzofurancarboxylic acid, 80 mg (0.53 mmol) of benzyl bromide, and 200 mg (1.45 mmol) of potassium carbonate in 4 ml of dimethylformamide was stirred at room temperature for 1 hour then diluted with diethyl ether and water. The organic phase was washed twice with water, dried over magnesium sulphate, evaporated to dryness and the residue chromatographed on silica gel using ethyl acetate/petrol (1:5) for the elution. There was obtained 104 mg of benzyl 2-[2-(tert-butoxyformamido)-2-methylpropyl]-5-benzofurancarboxylate as a colourless gum. ^1H NMR (400 MHz CDCl_3) δ : 1.39 (6H,s), 1.50 (9H,s), 3.23 (2H,s), 4.49 (1H,s), 5.41 (2H,s), 6.52 (1H,s), 7.34-7.52 (6H,m), 8.02 (1H,d), 8.30 (1H,s).

iv) 103 mg (0.24 mmol) of benzyl 2-[2-(tert-butoxyformamido)-2-methylpropyl]-5-benzofurancarboxylate were dissolved in 5 ml of trifluoroacetic acid/dichloromethane (1:1) for 10 minutes then evaporated to dryness and the residue dissolved in 1 ml of dimethylformamide and added to a stirred solution of 66 mg (0.25 mmol) of N-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamic acid, 115 mg (1 mmol) of N-ethylmorpholine, 45 mg (0.29 mmol) of 1-hydroxybenzotriazole hydrate and 70 mg (0.37 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride in 2 ml of dimethylformamide and the resulting mixture stirred at room temperature for 18 hours. After dilution with ethyl acetate the organic solution was washed with 2M hydrochloric acid, saturated sodium bicarbonate solution and water, dried over magnesium sulphate, evaporated to dryness and the residue chromatographed on silica gel using ethyl acetate/petrol (45:55) for the elution. After trituration with diethyl ether there was obtained 81 mg of benzyl 2-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]-5-benzofurancarboxylate as a white solid. MS m/e 568 [M+H]⁺.

Example 443

2-[3-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]phenoxy]acetic acid

A solution of 45 mg (0.081 mmol) of benzyl 2-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]phenoxy]acetate in 5 ml of ethanol/tetrahydrofuran (1:1) was hydrogenated with 4 mg of 10% palladium on carbon catalyst for 5 hours. The resulting suspension was filtered, evaporated to dryness and trituated with diethyl ether to give 29 mg of 2-[3-[2-[[[3-methoxy-4-(5-oxazolyl)amino]-2-methylpropyl]phenoxy]acetic acid as a white solid. MS: m/e 468 [M+H]⁺.

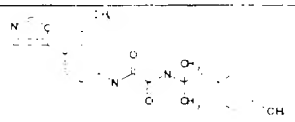
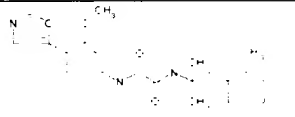
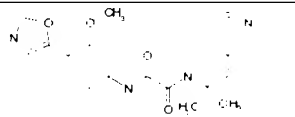
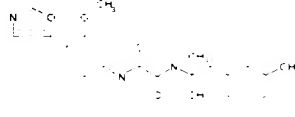
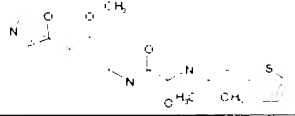
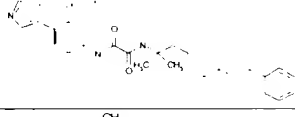
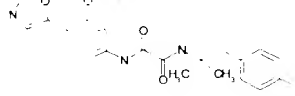
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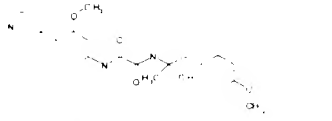
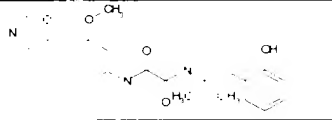
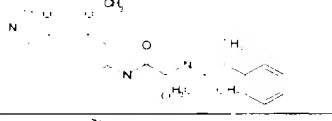
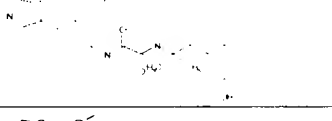
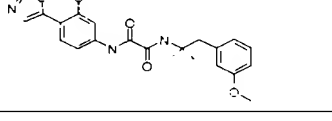
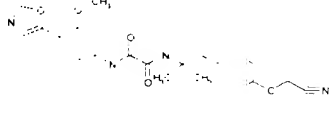
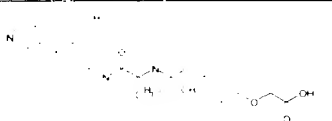
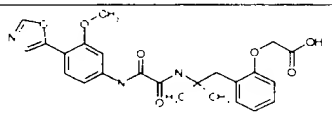
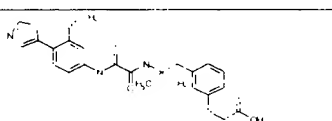
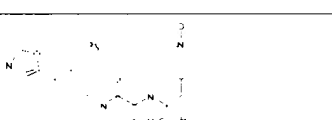
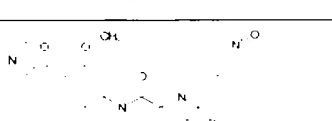
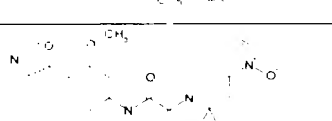
i) 8 mg (0.2 mmol) of 60% sodium hydride were added to a stirred solution of 85 mg (0.2 mmol) of N-[2-(3-hydroxyphenyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide in 1 ml of dimethylformamide. After 10 minutes 55 mg (0.24

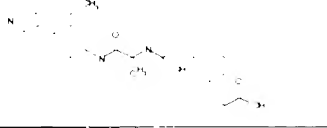
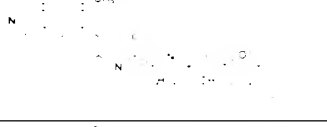
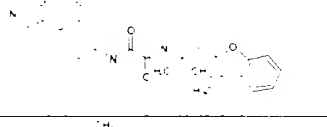
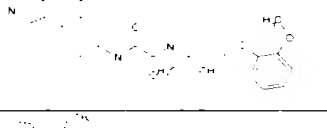
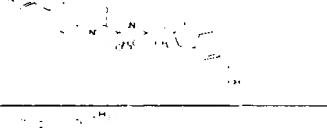
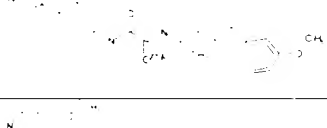
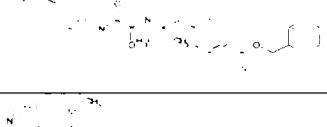
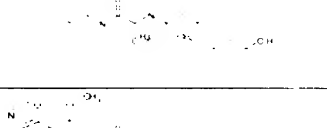
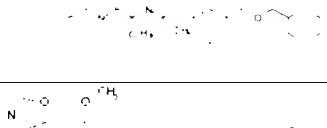
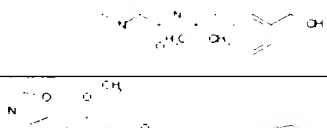
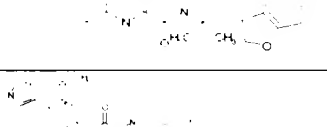
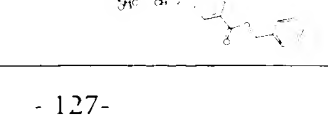
mmol) of benzyl bromoacetate were added and the mixture stirred at room temperature for 4 hours. The resulting solution was diluted with ethyl acetate, washed twice with water, dried over magnesium sulphate and evaporated to dryness. The residue was chromatographed on silica gel using ethyl acetate/petrol (2:1) for the elution. There was obtained 51 mg of benzyl 2-[3-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]phenoxy]acetate as a white solid. MS: m/e 558 [M+H]⁺.

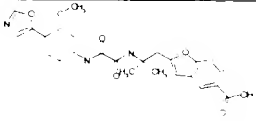
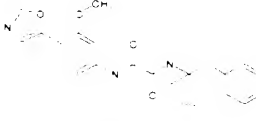
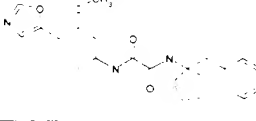
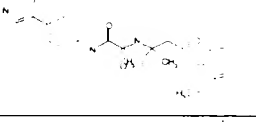
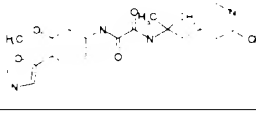
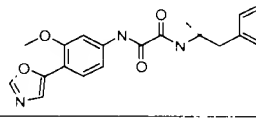
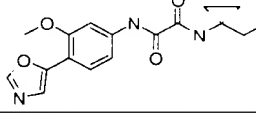
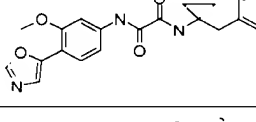
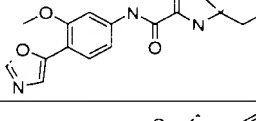
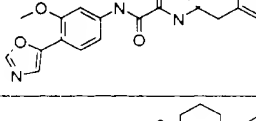
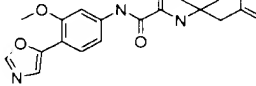
In a manner analogous to that described in Example 1, starting with N-[3-methoxy-4-(5-oxazolyl)phenyl] oxalamic acid, prepared as described in Example 1, parts (i) and (ii), and the appropriate amine, additional compounds shown in table 1c were also prepared.

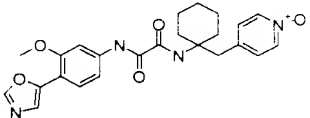
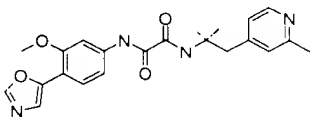
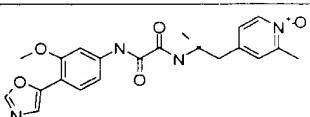
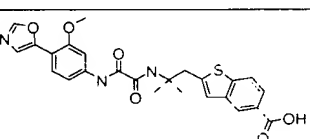
table 1c

Name	Structure	MS(ES) (M+H) ⁺	Ex No
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(4-methylphenyl)ethyl]oxalamide		408	302
N-[1,1-Dimethyl-2-(2-methylphenyl)ethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		408	303
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(3-pyridyl)ethyl]oxalamide		395	304
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(3-methylphenyl)ethyl]oxalamide		408	305
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(2-thienyl)ethyl]oxalamide		400	306
N-[2-(4-Benzyloxy-phenyl)-1,1-dimethyl-ethyl]-N'-(3-methoxy-4-oxazol-5-yl-phenyl)-oxalamide		500	307
N-[2-(4-Hydroxy-phenyl)-1,1-dimethyl-ethyl]-N'-(3-methoxy-4-oxazol-5-yl-phenyl)-oxalamide		410	308

N-(3-Methoxy-4-oxazol-5-yl-phenyl)-N'-[2-(4-methoxy-phenyl)-1,1-dimethyl-ethyl]-oxalamide		424	309
N-[2-(2-Hydroxy-phenyl)-1,1-dimethyl-ethyl]-N'-(3-methoxy-4-oxazol-5-yl-phenyl)-oxalamide		410	310
N-(1,1-Dimethyl-2-phenyl-propyl)-N'-(3-methoxy-4-oxazol-5-yl-phenyl)-oxalamide		408	311
N-[2-(3-Hydroxy-phenyl)-1,1-dimethyl-ethyl]-N'-(3-methoxy-4-oxazol-5-yl-phenyl)-oxalamide		410	312
N-(3-Methoxy-4-oxazol-5-yl-phenyl)-N'-[2-(3-methoxy-phenyl)-1,1-dimethyl-ethyl]-oxalamide		424	313
N-[2-[4-(Cyanomethoxy)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		449	314
2-[4-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]phenoxy]acetic acid		468	315
2-[2-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]phenoxy]acetic acid		468	438
2-[3-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]phenoxy]acetic acid		468	439
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(1-oxido-4-pyridyl)ethyl]oxalamide		411	440
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(1-oxido-3-pyridyl)ethyl]oxalamide		411	441
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(1-oxido-2-pyridyl)ethyl]oxalamide		411	442

2-[3-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]phenoxy]acetic acid		468	443
N-[2-(2-Benzofuranyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		434	444
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(3-methyl-2-benzofuranyl)ethyl]oxalamide		448	445
N-[2-(7-Methoxy-2-benzofuranyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		464	446
N-[2-(5-Methoxy-2-benzofuranyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		464	447
N-[2-(6-Methoxy-2-benzofuranyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		464	448
Benzyl 4-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]benzoate		528	449
4-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]benzoic acid		438	450
Benzyl 3-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]benzoate		528	451
3-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]benzoic acid		438	452
N-[2-(3-Benzofuranyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		434	453
Benzyl 2-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]-5-benzofurancarboxylate		568	454

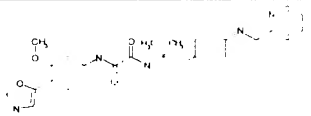
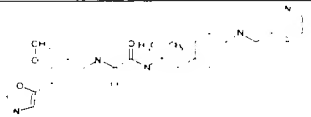
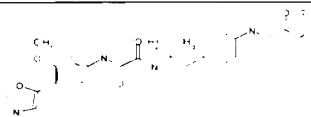
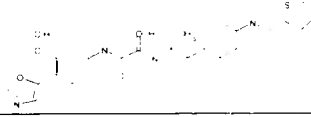
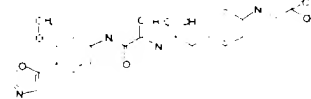
2-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]-5-benzofurancarboxylic acid		477.9	455
N-[3-Methoxy-4-(5-oxazolylphenyl)-N'-[1-[(4-pyridyl)methyl]-1-cyclopentyl]oxalamide		421	456
N-[3-Methoxy-4-(5-oxazolylphenyl)-N'-[1-[(1-oxido-4-pyridyl)methyl]-1-cyclopentyl]oxalamide		437	457
N-[2-(4-Methoxy-2-benzofuranyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		464	458
N'-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-(2,6-dimethyl-4-pyridyl)-1,1-dimethylethyl]oxalamide		423.22	653
N-[3-Methoxy-4-(5-oxazolylphenyl)-N'-[1,1-dimethyl-2-(2,6-dimethyl-1-oxido-4-pyridyl)ethyl]oxalamide		439.3	654
N-[3-Methoxy-4-(5-oxazolylphenyl)-N'-[1-[(4-pyridyl)methyl]-1-cyclopropyl]oxalamide		393	655
N-[3-Methoxy-4-(5-oxazolylphenyl)-N'-[1-[(1-oxido-4-pyridyl)methyl]-1-cyclopropyl]oxalamide		409	656
N-[3-Methoxy-4-(5-oxazolylphenyl)-N'-[1-[(4-pyridyl)methyl]-1-cyclobutyl]oxalamide		407	657
N-[3-Methoxy-4-(5-oxazolylphenyl)-N'-[1-[(1-oxido-4-pyridyl)methyl]-1-cyclobutyl]oxalamide		421	658
N-[3-Methoxy-4-(5-oxazolylphenyl)-N'-[1-[(4-pyridyl)methyl]-1-cyclohexyl]oxalamide		435	659


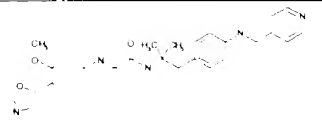
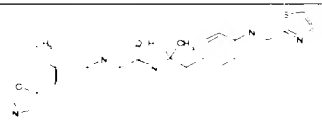
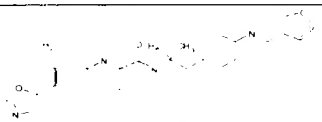

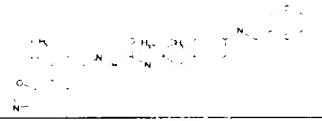
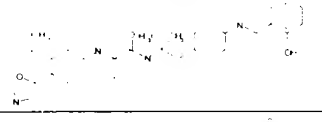
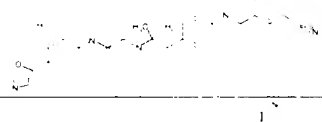
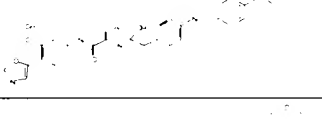

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1-[(1-oxido-4-pyridyl)methyl]-1-cyclohexyl]oxalamide		451	660
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(2-methyl-4-pyridyl)ethyl]oxalamide		409	661
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(2-methyl-1-oxido-4-pyridyl)ethyl]oxalamide		425	662
2-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]-5-benzothiophenecarboxylic acid		494	663

Examples 316-330:

In a manner analogous to that described in Example 11 starting with N-[2-(4-aminophenyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide, prepared as described in example 21, and the appropriate aldehyde compounds shown in table 1d were also prepared.

table 1d

Name	Structure	MS(ES) (M+H) ⁺	Ex No
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(2-pyridinyl)methylamino]phenyl]ethyl]oxalamide		500.1	316
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(3-pyridyl)methylamino]phenyl]ethyl]oxalamide		500.1	317
N-[2-[4-(2-Furfurylamino)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		489.1	318
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-Dimethyl-2-[4-(2-thenylamino)phenyl]ethyl]oxalamide		505.1	319
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2,2-dimethylpropylamino)phenyl]ethyl]oxalamide		479.2	320

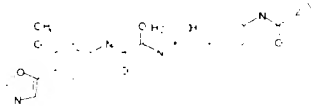
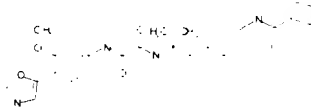
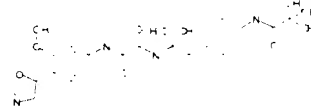
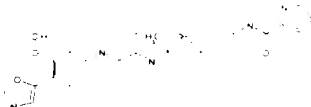
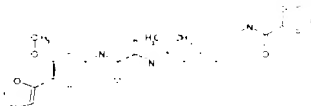
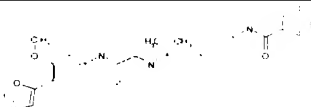
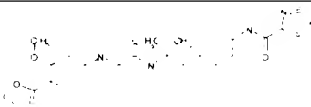
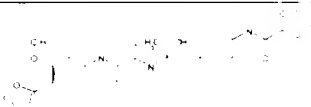
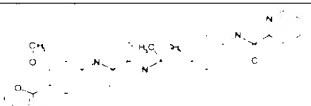
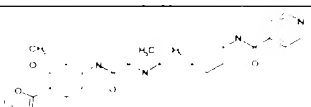
ide			
N-[2-[4-[(1H-Imidazol-2-yl)methylamino]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		489.1	321
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(4-pyridyl)methylamino]phenyl]ethyl]oxalamide		500.1	322
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(2-thiazolyl)methylamino]phenyl]ethyl]oxalamide		506.1	323
N-[2-[4-(3-Furfurylamino)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		489.1	324
N-[2-[4-[5-(Hydroxymethyl)-2-furfurylamino]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		519.1	325
N-[2-(4-Benzylaminophenyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		499.1	326
N-[2-[4-(2-Hydroxybenzylamino)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		515.1	327
N-[2-[4-(3-Cyanobenzylamino)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		524.1	328
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[4-(3-pyridyl)benzylamino]phenyl]ethyl]oxalamide		576.2	329
N-[2-[4-(2-Fluorobenzylamino)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		517.1	330



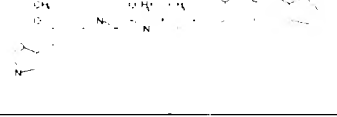
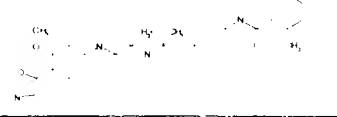
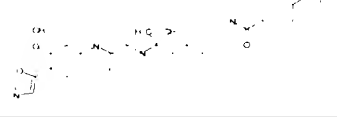
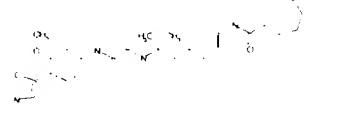
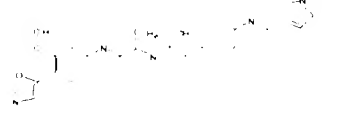
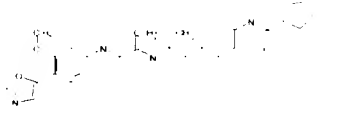
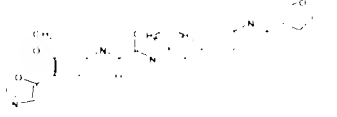

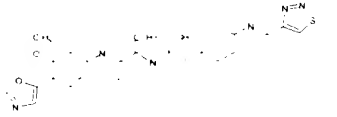
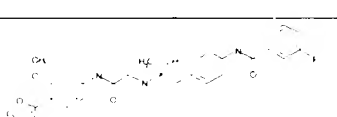
Examples 331-395 and 596-597 :

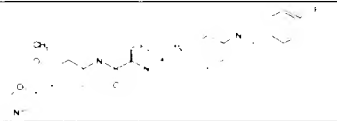

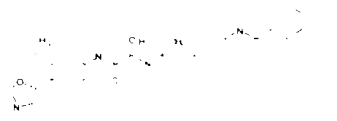

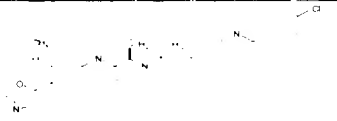
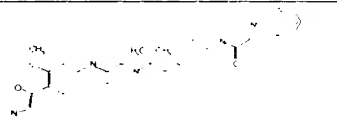
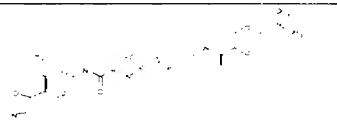
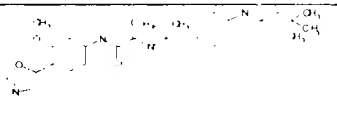
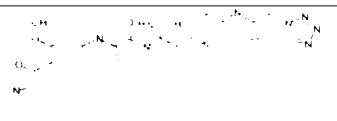
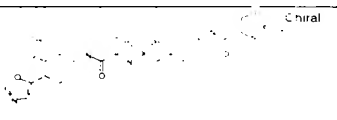
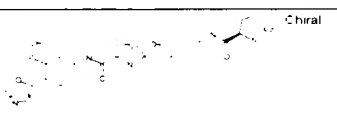
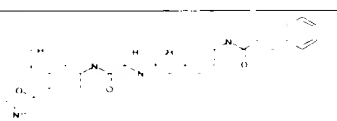
- In a manner analogous to that described in Example 22 starting from N-[2-(4-aminophenyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide, prepared as described in

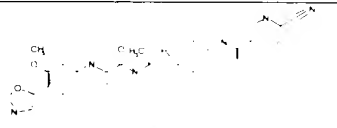
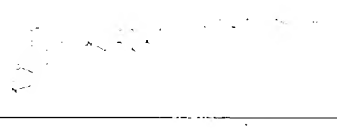
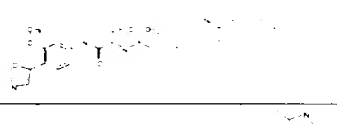

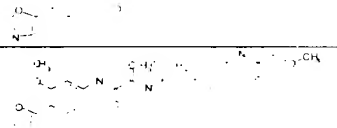
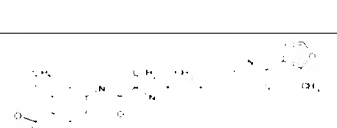
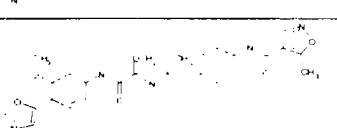

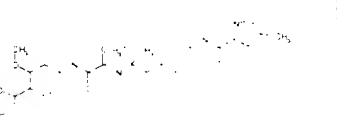
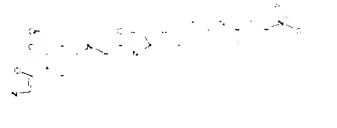
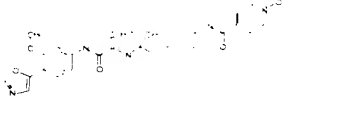

example 21, and the appropriate carboxylic acid compounds shown in table 1e were also prepared.

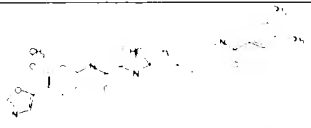

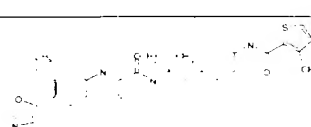
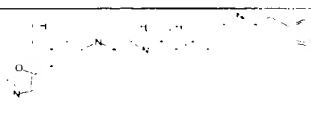
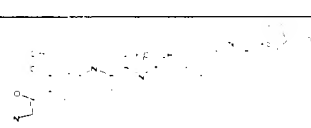
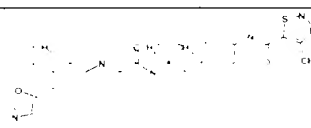
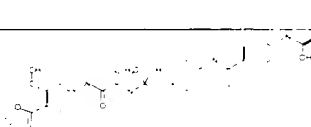
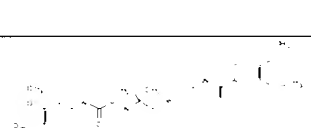
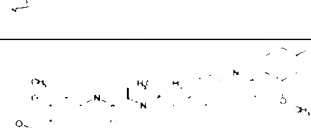
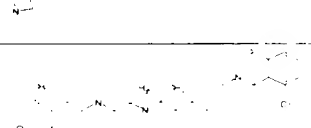
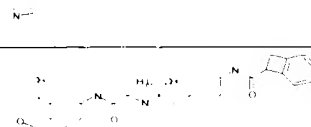
Table 1e


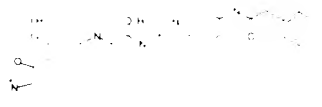

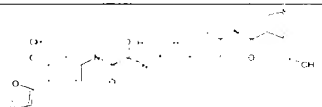


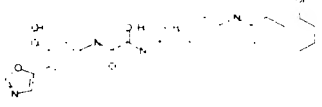
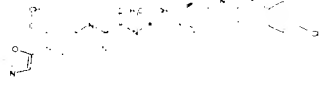
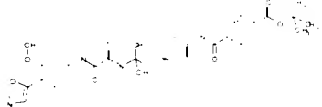
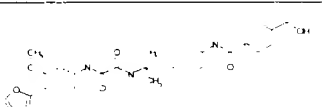
Name	Structure	MS(ES) (M+H) ⁺	Ex No
N-[2-[4-(Cyclopropylcarboxamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		477.1	331
N-[2-[4-(Cyclobutylcarboxamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		491.1	332
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(4-pivalamidophenyl)-1,1-dimethylethyl]oxalamide		493.1	333
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(1H-pyrrol-2-yl)carboxamido]phenyl]ethyl]oxalamide		502.1	334
N-[2-[4-[(2-Furyl)carboxamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		503.1	335
N-[2-[4-[(3-Furyl)carboxamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		503.1	336
N-[2-[4-[(1H-Imidazol-4-yl)carboxamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		503.1	337
N-[2-[4-[(Tetrahydro-2(RS)-furyl)carboxamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		507.2	338
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(2-pyridyl)carboxamido]phenyl]ethyl]oxalamide		514.1	339
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(4-pyridyl)carboxamido]phenyl]ethyl]oxalamide		514.1	340

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(2-thienyl)carboxamido]phenyl]ethyl]oxalamide		519.1	341
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(3-thienyl)carboxamido]phenyl]ethyl]oxalamide		519.1	342
N-[2-[4-(2-Cyclopentylacetamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		519.2	343
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-methylbenzamido)phenyl]ethyl]oxalamide		527.2	344
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(4-methylbenzamido)phenyl]ethyl]oxalamide		527.2	345
N-[2-[4-(Cycloheptylcarboxamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		533.2	346
N-[2-[4-[(5-Isoxazolyl)carboxamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		504.1	347
N-[2-[4-(Cyclopentylcarboxamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		505.2	348
N-[2-[4-[(Tetrahydro-3(RS)-furyl)carboxamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		507.1	349
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(1-methyl-1H-pyrrol-2-yl)carboxamido]phenyl]ethyl]oxalamide		516.1	350
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-(1,1-dimethyl-2-[4-[(1,2,3-thiadiazol-4-yl)carboxamido]phenyl]ethyl]oxalamide		521.1	351
N-[2-[4-(3-Fluorobenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		531.1	352

N-[2-[4-(4-Fluorobenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		531.1	353
N-[2-[4-(2-Methoxybenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		543.2	354
N-[2-[4-(2-Chlorobenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		547.1	355
N-[2-[4-(3-Chlorobenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		547.1	356
N-[2-[4-(4-Chlorobenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		547.1	357
N-[2-[4-[(1H-Indol-2-yl)carboxamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		552.1	358
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[4-(dimethylamino)benzamido]phenyl]ethyl]oxalamide		556.1	359
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(3,3-dimethylbutyramido)]phenyl]ethyl oxalamide		507.1	360
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[2-(1-tetrazolyl)acetamido]phenyl]ethyl]oxalamide		519.1	361
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(5-oxo-2(S)-pyrrolidinyl)carboxamido]phenyl]ethyl]oxalamide		520.1	362
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(5-oxo-2(R)-pyrrolidinyl)carboxamido]phenyl]ethyl]oxalamide		520.1	363
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(2-naphthyl)carboxamido]phenyl]ethyl]oxalamide		563.1	364

N-[2-[4-[(6-Cyano-3-pyridyl)carboxamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		580.1 (M+H+ ACN)	365
N-[2-[4-(3-Methoxybenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		543.1	366
N-[2-[4-(3,5-Difluorobenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		549.1	367
N-[2-[4-(1H-Indol-5-yl)carboxamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		552.1	368
(E)-N-[2-[4-(2-Butenamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		477.1	369
N-[2-[4-(2-Methoxyacetamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		481.2	370
N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(2-methyl-3-furyl)carboxamido]phenyl]ethyl]oxalamide		517.1	371
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(5-methyl-4-isoxazolyl)carboxamido]phenyl]ethyl]oxalamide		518.1	372
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(3-methyl-4-isoxazolyl)carboxamido]phenyl]ethyl]oxalamide		518.1	373
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(5-methyl-3-isoxazolyl)carboxamido]phenyl]ethyl]oxalamide		518.1	374
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N-[1,1-dimethyl-2-[4-[(1-oxido-3-pyridyl)carboxamido]phenyl]ethyl]oxalamide		530.1	375
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(1-oxido-4-pyridyl)carboxamido]phenyl]ethyl]oxalamide		530.1	376

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(4,5-dimethyl-2-furyl)carboxamido]phenyl]ethyl]oxalamide		531.1	377
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(2,5-dimethyl-2H-pyrazol-3-yl)carboxamido]phenyl]-1,1-dimethylethyl]oxalamide		531.1	378
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(3-methyl-2-thienyl)carboxamido]phenyl]ethyl]oxalamide		533.1	379
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[2-(3-thienyl)acetamido]phenyl]ethyl]oxalamide		533.1	380
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(4-methyl-2-thienyl)carboxamido]phenyl]ethyl]oxalamide		533.1	381
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(4-methyl-1,2,3-thiadiazol-5-yl)carboxamido]phenyl]ethyl]oxalamide		535	382
N-[2-[4-(4-Acetamidobenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		570.1	383
N-[2-[4-(3,4-Dimethoxybenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		573.1	384
N-[2-[4-(4-Chloro-2-methoxybenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		578.2	385
N-[2-[4-(2,6-Dichlorobenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		581	386
N-[2-[4-[(Bicyclo[4.2.0]octa-1(6),2,4-triene-7(RS)-yl)carboxamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		539.1	387

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-oxo-2-phenylacetamido)phenyl]ethyl]oxalamide		541.1	388
N-[2-{4-[2-(2-Fluorophenyl)acetamido]phenyl}-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		545	389
N-[2-{4-[2-(4-Fluorophenyl)acetamido]phenyl}-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		545	390
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N-[2-{4-[(4-methoxy-3-thienyl)carboxamido]phenyl}-1,1-dimethylethyl]oxalamide		549	391
N-[2-[4-(4-Acetylbenzamido)phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		555.1	392
N-[2-[4-[(1,3-Benzodioxol-5-yl)carboxamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		557.1	393
N-[2-[4-[2-(2-Chlorophenyl)acetamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		561.1	394
N-[2-[4-[2-(4-Chlorophenyl)acetamido]phenyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		561.1	395
tert-Butyl 4-[[4-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]phenyl]carbamoyl]benzoate		613	596
4-[[[4-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]phenyl]carbamoyl]benzoic acid		557	597

Examples 396-406 ; 433-437; 542-595 and 635-650

5 Typical methods used for the preparation of the compounds of tables 1f¹, 1f² and 1f³ are described below:

Example 398.

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(4-nitrophenoxy)propyl]oxalamide

- 5 (i) A mixture of 0.5g (3.94 mmol) of 2,4,4-trimethyl-5,6-dihydro-1,3(4H)oxazine and 0.5g (3.6 mmol) of 4-nitrophenol were heated at 180°C under a nitrogen atmosphere for 6 hours. The resulting mixture was cooled and purified by chromatography on silica gel using ethyl acetate for the elution. There was obtained 524 mg of N-[1,1-dimethyl-3-(4-nitrophenoxy)propyl]acetamide.
- 10 (ii) 693 mg (2.61 mmol) of N-[1,1-dimethyl-3-(4-nitrophenoxy)propyl]acetamide, 815 mg (2.87 mmol) of titanium isopropoxide and 719 mg (3.91 mmol) of diphenylsilane were dissolved in 8 ml of tetrahydrofuran and left at room temperature for 18 hours. The resulting solution was dissolved in ethyl acetate and saturated sodium bicarbonate solution, filtered and
- 15 the organic phase extracted twice with 2M hydrochloric acid. The combined acid extracts were basified with 2M sodium hydroxide solution, extracted with ethyl acetate and the organic extracts dried over magnesium sulphate, filtered and evaporated to dryness to give 266 mg of 1,1-dimethyl-3-(4-nitrophenoxy)propylamine. The 1,1-dimethyl-3-(4-nitrophenoxy)propylamine was then coupled to N-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamic acid by a procedure analogous to that described in example 1 to give N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(4-nitrophenoxy)propyl]oxalamide as a pale yellow solid. MS: m/e 469 [M+H]⁺.
- 20

Example 433

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4-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid.

- A solution of 650 mg (1.17 mmol) of benzyl 4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoate in 20 ml of tetrahydrofuran was
- 30 hydrogenated with 65 mg of 10% palladium on charcoal catalyst for 48 hours, a further 65 mg of catalyst being added after 24 hours and again after 44 hours. The resulting suspension was filtered, evaporated to dryness and the residue triturated with diethyl ether to give 415 mg of 4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid as a

white solid. MS: m/e 468 [M+H]⁺.

The starting material was prepared as follows:

- 5 i) A mixture of 1.14 g (5 mmol) of benzyl 4-hydroxybenzoate and 800 mg (6.3 mmol) of 2,4,4-trimethyl-5,6-dihydro-1,3(4H)-oxazine was stirred and heated at 180°C for 3 hours. A further 600 mg (4.72 mmol) of oxazine were added and heating was continued for 21 hours. The resulting mixture was cooled and chromatographed on silica gel using ethyl acetate/petrol (3:1) for the elution. There was obtained 1.52 g of benzyl 4-(3-acetamido-3-methylbutoxy) benzoate as a white solid. ¹H NMR (400 MHz CDCl₃) δ: 1.43 (6H,s), 1.94 (3H,s), 2.26 (2H,t), 4.14 (2H,t), 5.36 (2H,s), 5.65 (1H,s), 6.91 (2H,d), 7.35-7.52 (5H,m), 8.05 (2H,d).
- 10 ii) A solution of 1.5 g (4.23 mmol) of benzyl 4-(3-acetamido-3-methylbutoxy) benzoate, 1.166 g (6.35 mmol) of diphenylsilane and 1.2 g (4.23 mmol) of titanium(IV) isopropoxide in 4 ml of tetrahydrofuran was stirred at room temperature for 6 hours. The resulting mixture was diluted with diethyl ether/2M sodium hydroxide solution, filtered and the organic phase extracted twice with 2M hydrochloric acid. The combined aqueous extracts were basified with 2M sodium hydroxide solution and extracted with ether. The organic extract was dried over magnesium sulphate and evaporated to dryness to give 1.16 g of benzyl 4-(3-amino-3-methylbutoxy) benzoate as a pale coloured gum. ¹H NMR (400 MHz CDCl₃) δ: 1.22 (6H,s), 1.92 (2H,t), 4.08 (2H,t), 5.36 (2H,s), 6.90 (2H,d), 7.33-7.48 (5H,m), 8.05 (2H,d).
- 15 iii) A solution of 873 mg (3.33 mmol) of N-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamic acid, 500 mg (3.27 mmol) of 1-hydroxybenzotriazole hydrate, 1.2 g (3.83 mmol) of benzyl 4-(3-amino-3-methylbutoxy) benzoate and 1 g (5.22 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride in 10 ml of dimethylformamide was stirred at room temperature for 24 hours. The resulting mixture was diluted with ethyl acetate and washed with 2M hydrochloric acid, saturated sodium bicarbonate solution and water then dried over magnesium sulphate, evaporated to dryness and chromatographed on silica gel using ethyl acetate/petrol (2:1) for the elution. After trituration with diethyl ether there was obtained 765 mg of benzyl 4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoate as a white solid. MS: m/e 558 [M+H]⁺.
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Example 434

2-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid.

5

In an analogous manner to that described in Example 433 but replacing benzyl 4-[3-
[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoate with benzyl 2-
[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoate there was
obtained 2-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic
10 acid as a white solid. MS: m/e 468 [M+H]⁺.

The starting material was prepared as follows:

- i) A solution of 917 mg (3.5 mmol) of N-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamic
15 acid, 650 mg (4.66 mmol) of 3-amino-3-methyl-1-butanol hydrochloride (1:1), 612 mg (4
mmol) of 1-hydroxybenzotriazole hydrate, 690 mg (6 mmol) of N-ethylmorpholine and 960
mg (5 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride in 10 ml of
dimethylformamide was stirred at room temperature for 20 hrs. The resulting mixture was
diluted with ethyl acetate and washed with 2M hydrochloric acid, saturated sodium
20 bicarbonate solution and water then dried over magnesium sulphate, evaporated to dryness
and chromatographed on silica gel using ethyl acetate/petrol (3:1) for the elution. There was
obtained 410 mg of N-(3-hydroxy-1,1-dimethylpropyl)-N'-[3-methoxy-4-(5-
oxazolyl)phenyl]oxalamide as a pale yellow solid. MS: m/e 348 [M+H]⁺.
- 25 ii) A solution of 48 mg (0.276 mmol) of diethyl azodicarboxylate in 2 ml of
tetrahydrofuran was added to a mixture of 72 mg (0.275 mmol) of triphenylphosphine, 57 mg
(0.25 mmol) of benzyl salicylate and 87 mg (0.25 mmol) of N-(3-hydroxy-1,1-
dimethylpropyl)-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide and left at room
temperature for 1 hour. The resulting mixture was chromatographed twice on silica gel using
30 first ethyl acetate/petrol (1:1) then methanol/dichloromethane (1:49) for the elutions. There
was obtained 29 mg of benzyl 2-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-
methylbutoxy]benzoate as a colourless gum. MS: m/e 558 [M+H]⁺.

Example 435

3-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid.

5 In an analogous manner to that described in Example 433 but replacing benzyl 4-hydroxybenzoate with benzyl 3-hydroxybenzoate there was obtained 3-[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid as a white solid. MS: m/e 468 [M+H]⁺.

Example 553

4-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropoxy]benzoic acid.

15 In an analogous manner to that described in Example 433 but replacing benzyl 4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoate with benzyl 4-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropoxy]benzoate there was obtained 4-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropoxy]benzoic acid as a white solid. MS: m/e 454 [M+H]⁺.

20 The starting material was prepared as follows:

(i) A solution of 0.280 g (4 mmol) of 2,2-dimethylaziridine (Cairns, J. Am. Chem. Soc. 1941, 63, 871) and 9 g (40 mmol) of benzyl 4-hydroxybenzoate in 30 ml of chloroform was heated under reflux for 3 hr. The reaction mixture was allowed to cool and diluted with dichloromethane. The solution was washed with 2M sodium hydroxide solution, dried over anhydrous magnesium sulphate, and concentrated *in vacuo*. Column chromatography of the residue using (dichloromethane:methanol:acetic acid:water (240:12:3:2) afforded benzyl 4-(2-amino-2-methylpropoxy)benzoate (0.300g, 1 mmol, 25%).

(ii) The benzyl 4-(2-amino-2-methylpropoxy)benzoate was coupled to N-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamic acid in a manner analogous to that described for example 433,

part (iii) to give benzyl 4-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropoxy]benzoate as a white solid.

Example 561 was prepared in a manner analogous to that described for example 433, parts (i) and (ii) where the benzyl 4-hydroxybenzoate was replaced with 3-cyanophenol.

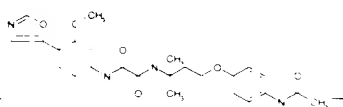
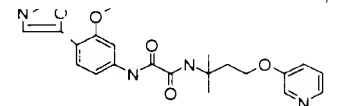
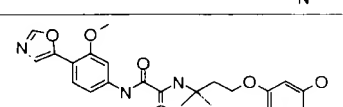
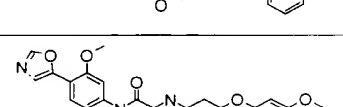
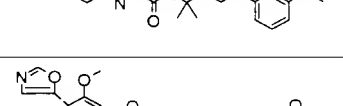
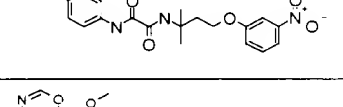
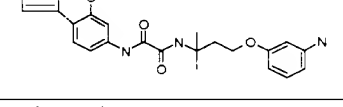
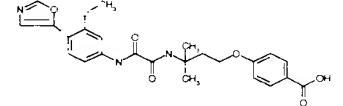
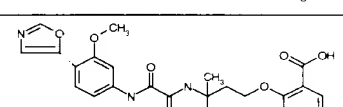
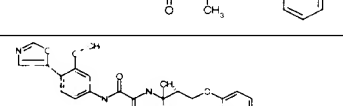
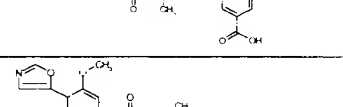
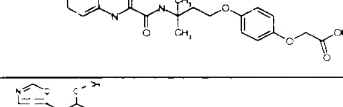
Examples 585, 588 and 589 were prepared from the compounds of examples 583, 587 and 586 respectively, by reacting the nitrile substituent with trimethylsilyl azide and dibutyl tin oxide according to the method of S.J. Wittenberger and B.G.J. Donner, J. Org. Chem., 1993, 58, 4139-4141.

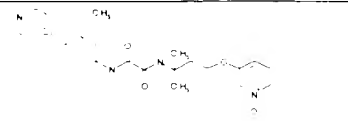
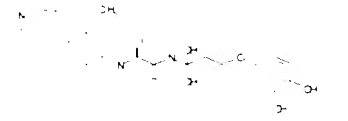
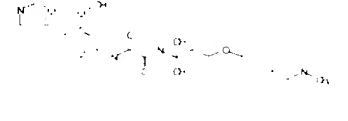
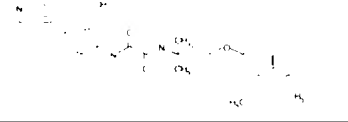

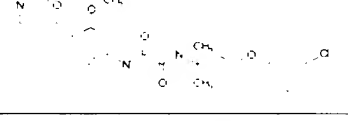

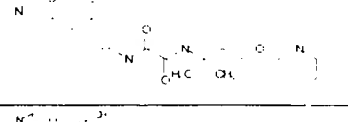
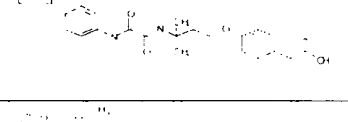
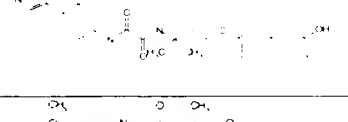
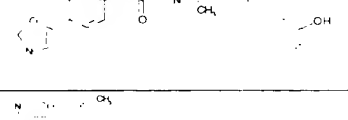

For examples in table 1f¹ containing unprotected hydroxyl or amino groups suitable protecting groups were used, such as benzyl for hydroxyl and benzyloxycarbonyl for amino or similar groups, hereinbefore mentioned and well known in the art.


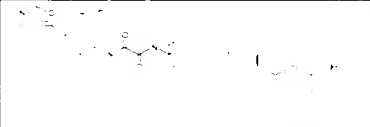
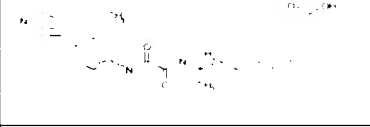
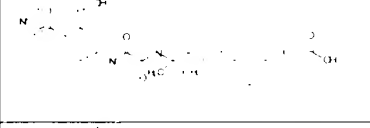
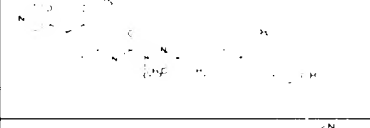
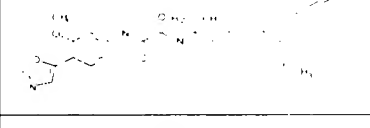
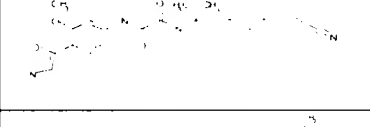
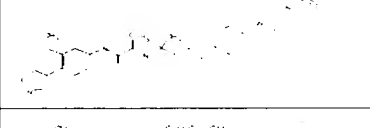
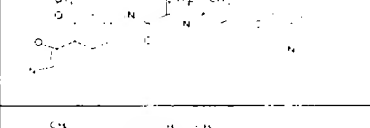
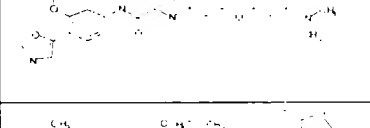
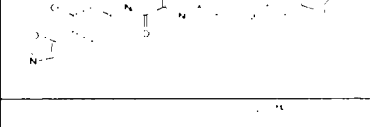
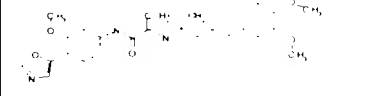
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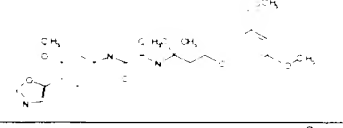
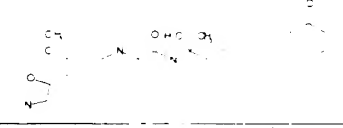
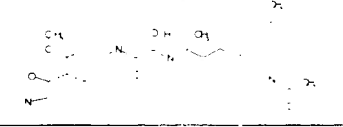
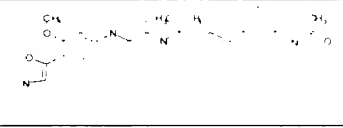
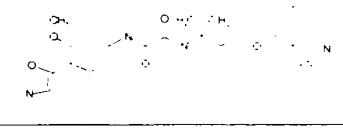
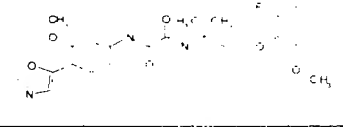

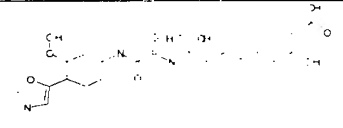
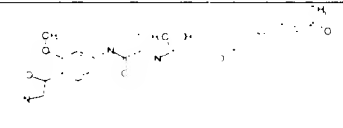
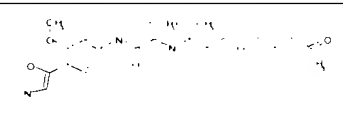
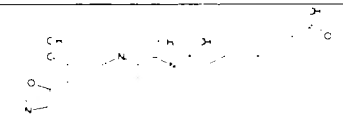
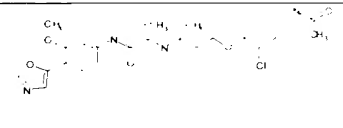
table 1f¹

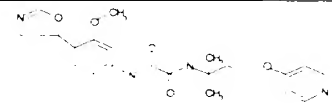
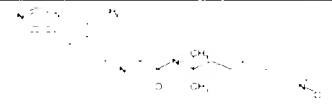
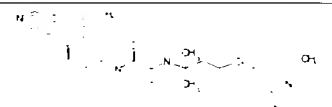
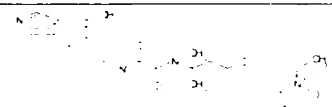
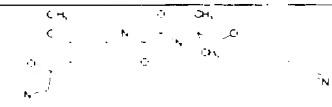
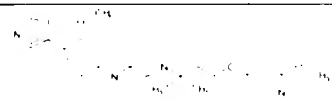
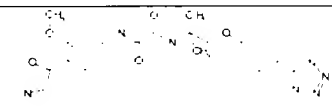
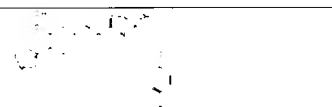
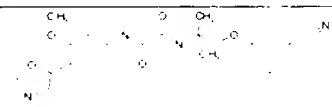
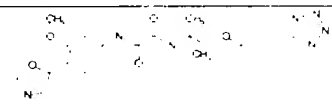
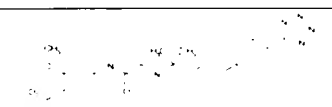
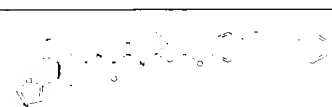
Name	Structure	MS(ES) (M+H) ⁺	Ex No
N-[3-(4-Hydroxy-phenoxy)-1,1-dimethyl-propyl]-N'-(3-methoxy-4-oxazol-5-yl-phenyl)-oxalamide		440	396
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[3-(4-methoxyphenoxy)-1,1-dimethylpropyl]oxalamide		454	397
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(4-nitrophenoxy)propyl]oxalamide		469	398
N-[3-(2-Hydroxyphenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		440	399
N-[3-(4-Amino-phenoxy)-1,1-dimethyl-propyl]-N'-(3-methoxy-4-oxazol-5-yl-phenyl)-oxalamide		439	400




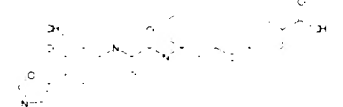


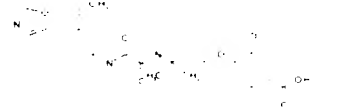
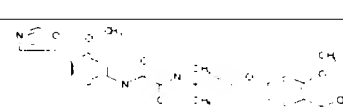
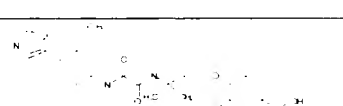
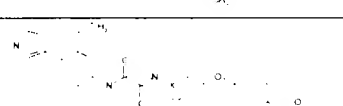
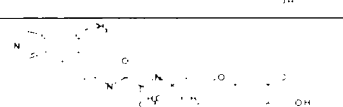
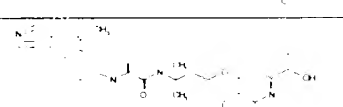
N-[3-(4-Acetylamino-phenoxy)-1,1-dimethyl-propyl]-N'-(3-methoxy-4-oxazol-5-yl-phenyl)-oxalamide		481	401
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(3-pyridyloxy)propyl]oxalamide		425	402
N-[3-(3-Hydroxyphenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		440	403
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[3-(3-methoxyphenoxy)-1,1-dimethylpropyl]oxalamide		454	404
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(3-nitrophenoxy)propyl]oxalamide		469	405
N-[3-(3-Aminophenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		439	406
4-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid		468	433
2-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid		468	434
3-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid		468	435
2-[4-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]phenoxy]acetic acid		498	436
2-[2-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]phenoxy]acetic acid		498	437
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-(1,1-dimethyl-3-phenoxypropyl)oxalamide		424	542

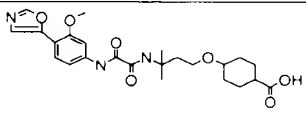
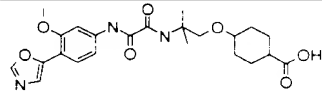
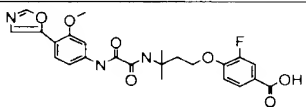
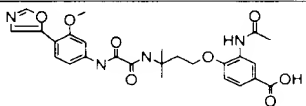
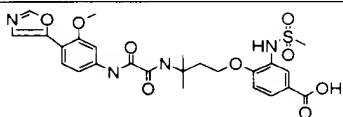
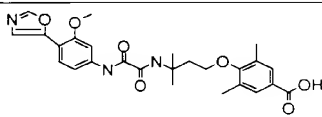
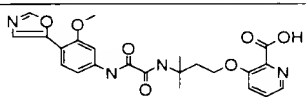
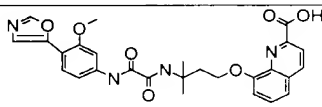
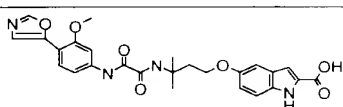
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(1-oxido-3-pyridyloxy)propyl]oxalamide		441	543
N-[3-(3,4-Dihydroxyphenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		456	544
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-[4-(methylcarbamoyl)phenoxy]propyl]oxalamide		481	545
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[3-(3,4-dimethoxyphenoxy)-1,1-dimethylpropyl]oxalamide		484	546
N-[3-[4-[(2-Hydroxyethyl)carbamoyl]phenoxy]-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		511	547
N-[3-(3-Chlorophenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		458	548
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(3-pyridyloxy)propyl]oxalamide		425	549
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(2-pyridyloxy)propyl]oxalamide		425	550
2-[4-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]phenyl]acetic acid		482	551
2-[3-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]phenyl]acetic acid		482	552
4-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropoxy]benzoic acid		454	553
4-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]-2-methylbenzoic acid		482	554

3-[3-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]phenyl]propionic acid		496	555
3-[4-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]phenyl]propionic acid		496	556
3-[2-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]phenyl]propionic acid		496	557
2-[3-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]phenoxy]acetic acid		498	558
4-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]-3-methylbenzoic acid		482	559
N-[3-(4-Cyano-2-methoxyphenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		479	560
N-[3-(3-Cyanophenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		449.6	561
N-[3-[4-(4-Acetyl-1-piperazinyl)phenoxy]-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		550.4	562
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(2-morpholinophenoxy)propyl]oxalamide		531.4 (M + Na) ⁺	563
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-[3-(dimethylamino)phenoxy]propyl]oxalamide		489.6 (M + Na) ⁺	564
N-[3-(1,3-Benzodioxol-5-yloxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		468.4	565
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[3-(3,4,5-trimethoxyphenoxy)-1,1-dimethylpropyl]oxalamide		514.4	566

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[3-(3,5-dimethoxyphenoxy)-1,1-dimethylpropyl]oxalamide		506 (M + Na) ⁺	567
N-[3-(5,6,7,8-Tetrahydro-5-oxo-2-naphthyloxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		492.4	568
N-[3-(2-Acetamido-5-methylphenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		517.6 (M + Na) ⁺	569
N-[3-(3-Acetamidophenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		503.6 (M + Na) ⁺	570
N-[3-(1H-Indol-4-yloxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		485.2 (M + Na) ⁺	571
N-[3-(2-Fluoro-6-methoxyphenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		472.2	572
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(2-oxo-2H-1-benzopyran-7-yloxy)propyl]oxalamide		492.4	573
N-[3-(4-Acetyl-3-methylphenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		480.2	574
(E)-N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-[4-(3-oxo-1-butenyl)phenoxy]propyl]oxalamide		492.4	575
N-[3-(3-Acetylphenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		466.4	576
N-[3-(4-Acetylphenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		466.2	577
N-[3-(4-Acetamido-2-chlorophenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		515.6	578

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(4-pyridyloxy)propyl]oxalamide		425	579
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(1-oxido-4-pyridyloxy)propyl]oxalamide		441	580
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(2,6-dimethyl-4-pyridyloxy)propyl]oxalamide		453	581
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(2,6-dimethyl-1-oxido-4-pyridyloxy)propyl]oxalamide		469	582
N-[2-(4-Cyanophenoxy)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		435	583
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[3-(2-methoxy-4-pyridyloxy)-1,1-dimethylpropyl]oxalamide		455	584
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(1H-tetrazol-5-yl)phenoxy]ethyl]oxalamide		478	585
N-[3-(4-Cyanophenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		449	586
N-[2-(3-Cyanophenoxy)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		476	587
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[3-(1H-tetrazol-5-yl)phenoxy]ethyl]oxalamide		478	588
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-[4-(1H-tetrazol-5-yl)phenoxy]propyl]oxalamide		492	589
Benzyl 4-[2-[1-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-1-cyclobutyl]ethoxy]benzoate		570.2	590

Benzyl 4-[2-[1-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-1-cyclopentyl]ethoxy]benzoate		584.3	591
Benzyl 4-[2-[1-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-1-cyclohexyl]ethoxy]benzoate		598.3	592
4-[2-[1-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-1-cyclopentyl]ethoxy]benzoic acid		494.2	593
4-[2-[1-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-1-cyclohexyl]ethoxy]benzoic acid		508.2	594
4-[2-[1-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-1-cyclobutyl]ethoxy]benzoic acid		480.2	595
Benzyl 2-methoxy-4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoate		588	635
3-Chloro-4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid		502	636
2-Methoxy-4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid		498	637
3-Methoxy-4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid		498	638
4-[2-[1-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-1-cyclopropyl]ethoxy]benzoic acid		466	639
2-Chloro-4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid		502	640
4-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]-2-quinolinecarboxylic acid		519	641

(cis/trans)-4-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]-1-cyclohexanecarboxylic acid		474	642
(cis/trans)-4-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropoxy]-1-cyclohexanecarboxylic acid		460	643
3-Fluoro-4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid		486	644
3-Acetamido-4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid		525	645
3-(Methanesulfonamido)-4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid		561	646
4-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]-3,5-dimethylbenzoic acid		496	647
3-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]-2-pyridinecarboxylic acid		469	648
8-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]-2-quinolinecarboxylic acid		519	649
5-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]-2-indolecarboxylic acid		507	650

Examples 615-631 and 664-670

5 Example 615

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(phenylthio)ethyl]oxalamide.

- (i) A mixture of 2g (17.7 mmol) of 2,4,4-trimethyl-2-oxazoline and 1.95 g (17.7 mmol) of thiophenol were heated at 120°C for 18 hours. After cooling the resulting solid was triturated

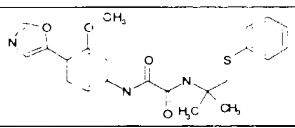
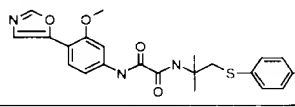
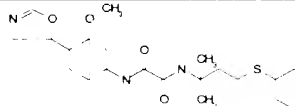
with diethyl ether/petrol (1:2) and filtered off to give 2.55 g of N-[1,1-dimethyl-2-(phenylthio)ethyl]acetamide as a white solid.

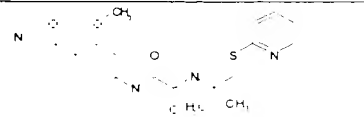
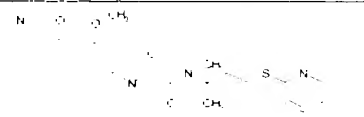
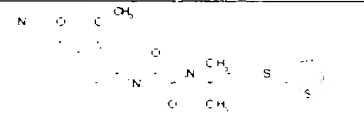
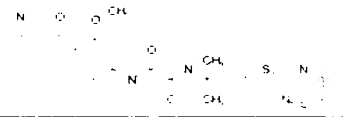
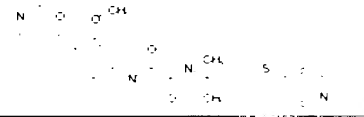
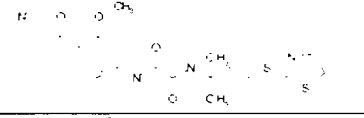
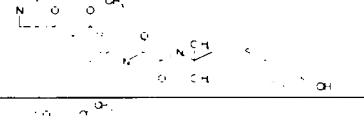
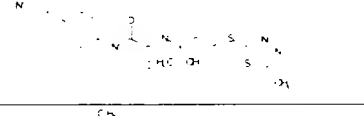
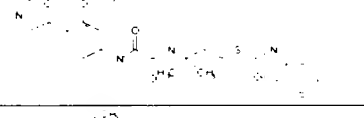
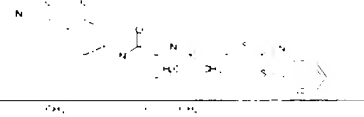
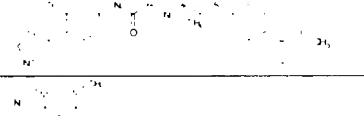
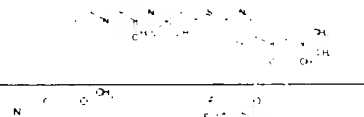
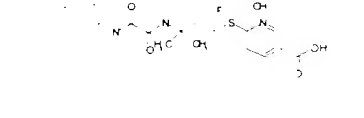
(ii) A solution of 2.5 g (11.2 mmol) of N-[1,1-dimethyl-2-(phenylthio)ethyl]acetamide, 3.18 g (11.2 mmol) of titanium isopropoxide and 3.09 g (16.8 mmol) of diphenylsilane in 12 ml of tetrahydrofuran were stirred at room temperature for 18 hours. The resulting mixture was chromatographed on silica gel using 3%, 6% and 10% methanol in dichloromethane for the elution. There was obtained 2 g of 1,1-dimethyl-2-(phenylthio)ethylamine as a pale orange oil. The 1,1-dimethyl-2-(phenylthio)ethylamine was then coupled to N-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamic acid by a procedure analogous to that described in example 1 to afford N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(phenylthio)ethyl]oxalamide. MS: m/e 426 [M+H]⁺.

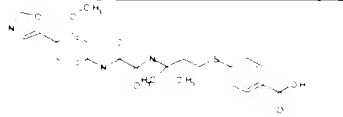
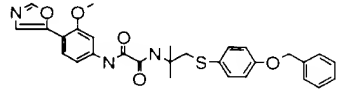
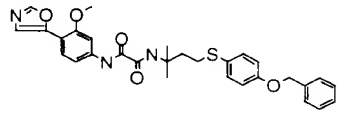
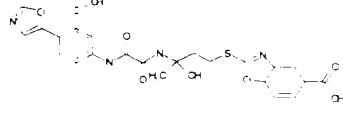
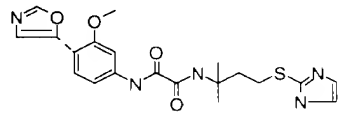
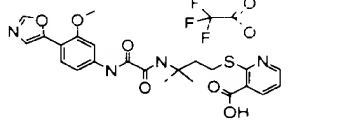
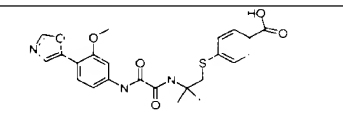
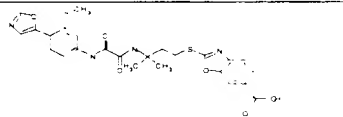
Example 616 was prepared by an analogous method to that described for example 615 but using 4-benzyloxythiophenol in place of the thiophenol and removing the protecting group using a mixture of hydrogen bromide in acetic acid.

The additional compounds in table 1f² were prepared in an analogous manner to that described for example 615 by reaction of the appropriate thiol with either 2,4,4-trimethyl-2-oxazoline or 2,4,4-trimethyl-5,6-dihydro-1,3(4H)oxazine and, where necessary, removal of any protecting groups by conventional methods.

table 1f²

Name	Structure	MS(ES) (M+H) ⁺	Ex No
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(phenylthio)ethyl]oxalamide		426	615
N-[2-(4-Hydroxyphenylthio)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		442	616
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(phenylthio)ethyl]oxalamide		440	617

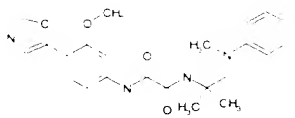
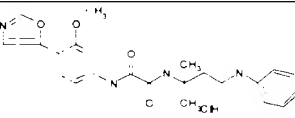
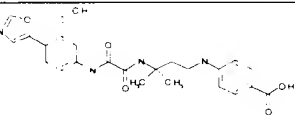
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(2-pyridylthio)ethyl]oxalamide		427	618
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(2-pyridylthio)propyl]oxalamide		441	619
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(2-thienylthio)propyl]oxalamide		446	620
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(2-pyrimidylthio)propyl]oxalamide		442	621
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(4-pyridylthio)propyl]oxalamide		441	622
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(2-thiazolylthio)propyl]oxalamide		447	623
N-[3-(4-Hydroxyphenylthio)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		456	624
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(5-methyl-1,3,4-thiadiazol-2-ylthio)propyl]oxalamide		462	625
N-[3-(2-Benzooxazolylthio)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		481	626
N-[3-(2-Benzothiazolylthio)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		497	627
Methyl 4-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropylthio]benzoate		484	628
tert-Butyl 6-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutylthio]-3-pyridinecarboxylate		541	629
6-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutylthio]-3-pyridinecarboxylic acid trifluoroacetate (1:1)		485	630

4-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutylthio]benzoic acid		484	631
N-[2-(4-Benzyloxyphenylthio)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		532	664
N-[2-(4-Benzyloxyphenylthio)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		546	665
2-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutylthio]-5-benzoxazolecarboxylic acid		525	666
N-[3-(1H-Imidazol-2-ylthio)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		430	667
2-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutylthio]-3-pyridinecarboxylic acid trifluoroacetate (1:1)		485	668
4-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropylthio]benzoic acid		470	669
2-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutylthio]-6-benzoxazolecarboxylic acid		525	670

Examples 632-634

The compounds in table 1f³ were prepared in an analogous manner to that described for example 398 in table 1f¹ by replacing the 4-nitrophenol with the appropriate aniline and reaction with either 2,4,4-trimethyl-2-oxazoline or 2,4,4-trimethyl-5,6-dihydro-1,3(4H)oxazine and, where necessary, removal of any protecting groups by conventional methods.

table 1f³

Name	Structure	MS(ES) (M+H) ⁺	Ex No
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(N-methylanilino) ethyl] oxalamide		423	632
N-(3-Anilino-1,1-dimethylpropyl)-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide hydrochloride (1:1)		423	633
4-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutylamino]benzoic acid		467	634

Examples 407-414; 459-541 and 651-652

- 5 Typical methods used for the preparation of the compounds of table 1g are described below:

Example 408.

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(4-methoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide.

10

- (i) A stirred solution of 3.23 g (16.8 mmol) of 1-(4-methoxyphenyl)piperazine, 2.00 g (16.8 mmol) of 2-methyl-2-nitropropan-1-ol and 5.34 g (50.4 mmol) of sodium carbonate in 40ml of n-butanol was refluxed for 16h. The reaction mixture was allowed to cool and diluted with 100ml of dichloromethane. The solution was filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel using petroleum ether/ethyl acetate (10:1) for the elution to afford 1.86 g (6.34 mmol, 38%) of 1-(4-methoxyphenyl)-4-(2-methyl-2-nitropropyl)piperazine as a white solid.
- 15 (ii) A solution of 1.86 g (6.34 mmol) of 1-(4-methoxyphenyl)-4-(2-methyl-2-nitropropyl)piperazine and 0.5 g of palladium on activated charcoal in 50 ml of ethanol was stirred at room temperature under an atmosphere of hydrogen for 48h. The reaction mixture was filtered and the filtrate concentrated in vacuo to afford 1.59 g (6.04 g mmol, 95%) of 2-[4-(4-methoxyphenyl)-piperazin-1-yl]-1,1-dimethylethylamine as a clear oil. The 2-[4-(4-methoxyphenyl)-piperazin-1-yl]-1,1-dimethylethylamine was then coupled to N-[3-methoxy-4-(5-oxazolyl)phenyl] oxalamic acid by a procedure analogous to that described in example 1 to
- 20

afford N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(4-methoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide as a white solid. MS: m/e 508 [M+H]⁺.

5 Examples 407, 409, 410, 411, 412 and similar structures were prepared by an analogous procedure by replacing the 1-(4-methoxyphenyl)piperazine with the appropriately substituted piperazine.

10 Examples 413 and 414 were prepared by an analogous procedure by replacing the 1-(4-methoxyphenyl)piperazine with t-butyl-1-piperazinecarboxylate to give 4-(2-amino-2-methylpropyl)piperazine-1-carboxylic acid t-butyl ester which was then coupled to N-[3-methoxy-4-(5-oxazolyl)phenyl]oxamic acid. The resulting product could then be deprotected to give N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(1-piperazinyl)ethyl]oxalamide that could be used for the preparation of examples 413, 414 and a variety of additional N-acyl and N-sulfonyl derivatives, such as those shown in table 1g, by
15 using the appropriate acylating or sulfonylating reagent.

Example 489.

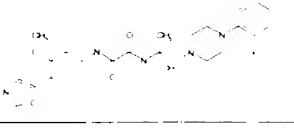

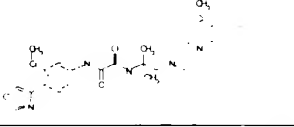

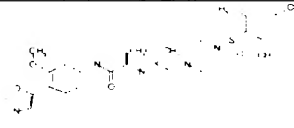
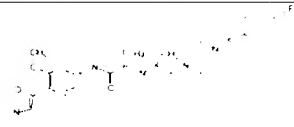
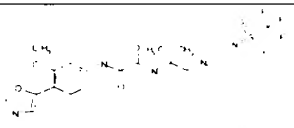

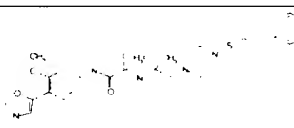
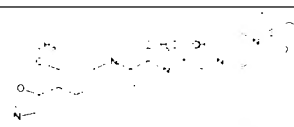
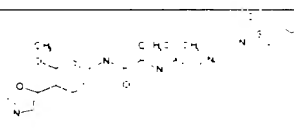
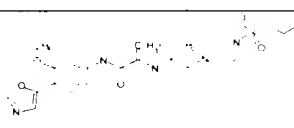
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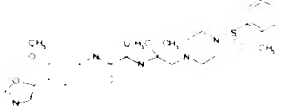
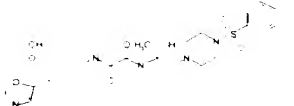
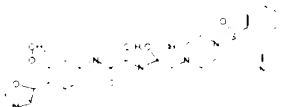
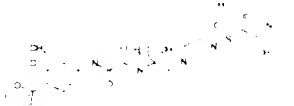
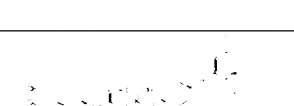

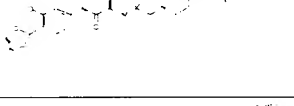
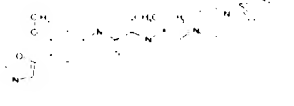
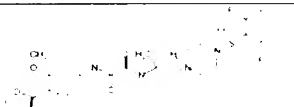
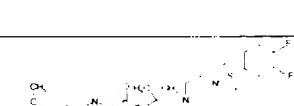
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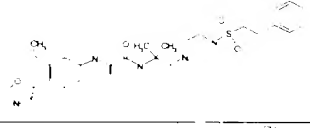
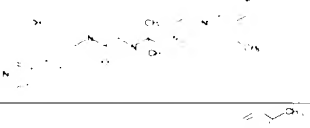
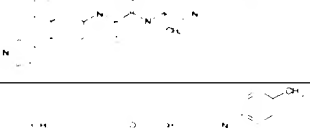
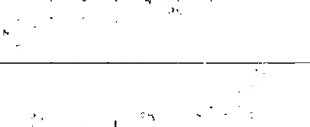
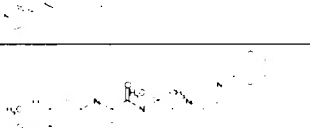
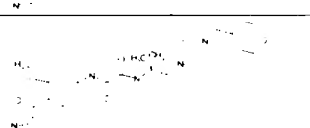
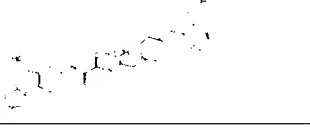
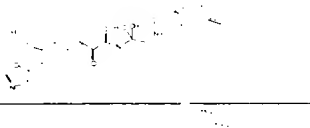
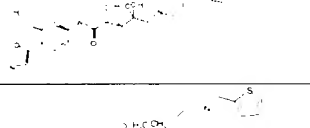
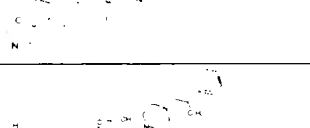


A stirred solution of 48mg of N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(1-piperazinyl)ethyl]oxalamide (1.2mmol) and 13mg of cyclohexanecarboxaldehyde (1.2mmol) in 1ml of a 5% acetic acid / dichloromethane mixture was treated with a solution of 38mg of sodium triacetoxyborohydride (1.8mmol) in 1ml of a 5% acetic acid / dichloromethane
25 mixture. After stirring overnight at room temperature the reaction mixture was diluted with 10ml of dichloromethane and washed with 8ml of a sodium bicarbonate solution followed by 8ml of water. The organic layer was then evaporated and purified using flash chromatography on a silica gel column eluting with 5% methanol / dichloromethane to give after evaporation of the fractions 14.3mg (0.3 mmol, 25%) of N-[2-[4-(cyclohexylmethyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide in the form of a white solid.
30 MS: m/e 498.2 [M+H]⁺.



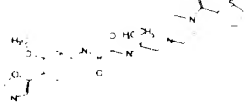
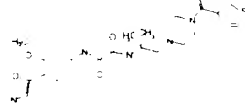
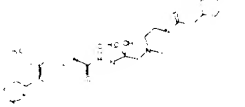
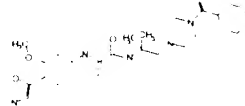
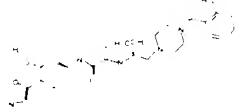
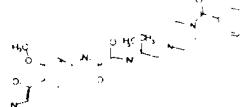
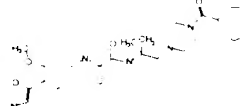
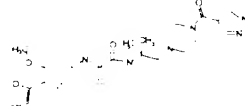
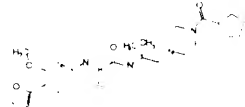
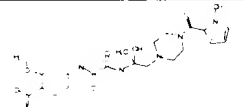
Additional N-alkylated compounds shown in table 1g were prepared by analogous methods.

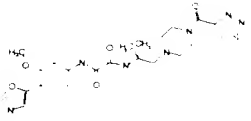

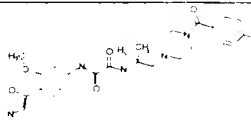
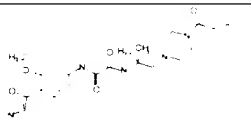
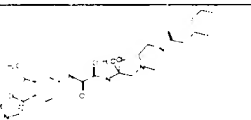
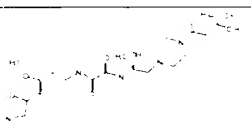
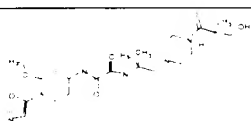
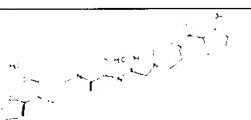
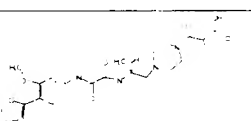
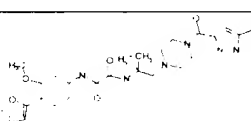
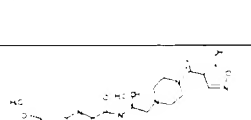
table 1g			
Name	Structure	MS(ES) (M+H) ⁺	Ex No
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(4-phenyl-1-piperazinyl)ethyl]oxalamide		478	407
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(4-methoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide		508	408
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(3-methoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide		508	409
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(4-phenyl-1-piperazinyl)propyl]oxalamide		492	410
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide		508	411
N-[2-(4-Benzyl-1-piperazinyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		492	412
N-[2-[4-(Benzenesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		452	413
N-[2-(4-Benzoyl-1-piperazinyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		506	414
N-[2-[4-[4-(Trifluoromethyl)phenyl]-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		546	459
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]oxalamide		492	460


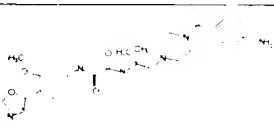
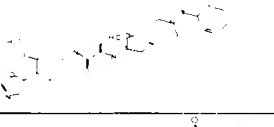
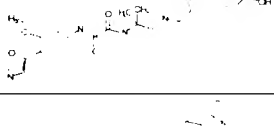
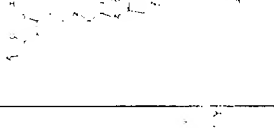
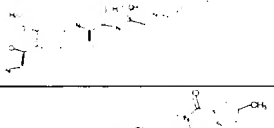
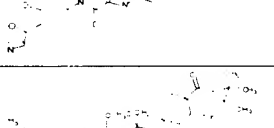

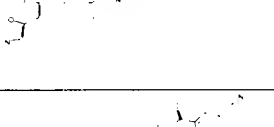
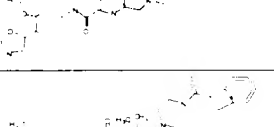
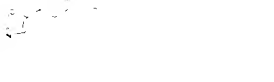
N-[2-[4-(2-Fluorophenyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		496	461
N-[2-[4-(4-Fluorophenyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		496	462
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide		508	463
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-thiophenesulfonyl)-1-piperazinyl]ethyl]oxalamide		548	464
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2,4,6-trimethylbenzenesulfonyl)-1-piperazinyl]ethyl]oxalamide		584.1	465
N-[2-[4-(4-Fluorobenzenesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		560.1	466
N-[2-[4-(Trifluoromethanesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		534	467
N-[2-[4-(Isopropylsulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		508.1	468
(E)-N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(styrylsulfonyl)-1-piperazinyl]ethyl]oxalamide		568.1	469
N-[2-[4-(Ethanedisulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		494.1	470
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(propanedisulfonyl)-1-piperazinyl]ethyl]oxalamide		508.1	471
N-[2-[4-(3-Chloropropanedisulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		542.1	472

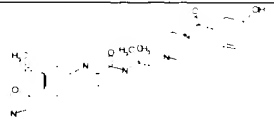
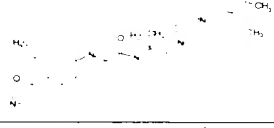
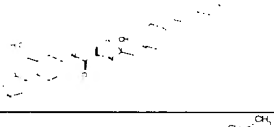
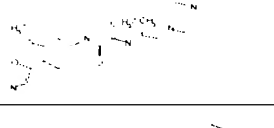
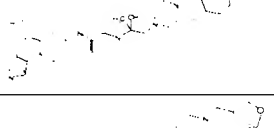
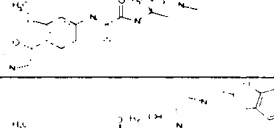
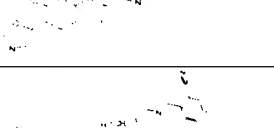
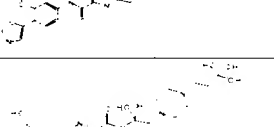
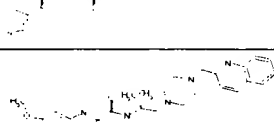
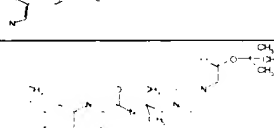
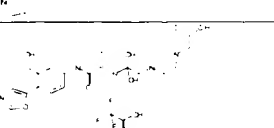
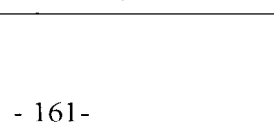
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(o-toluenesulfonyl)-1-piperazinyl]ethyl]oxalamide		556.1	473
N-[2-[4-(2-Fluorobenzenesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		560.1	474
N-[2-[4-(2-Cyanobenzenesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		567.1	475
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(3,5-dimethyl-4-isoxazolsulfonyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide		561.1	476
N-[2-[4-(5-Fluoro-2-methylbenzenesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		574.1	477
N-[2-[4-(2,5-Difluorobenzenesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		578.1	478
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(1-methyl-1H-imidazole-4-sulfonyl)-1-piperazinyl]ethyl]oxalamide		546.1	479
N-[2-[4-(2,6-Difluorobenzenesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		578.1	480
N-[2-[4-(3,4-Difluorobenzenesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		578.1	481
N-[2-[4-(Cyclohexylmethanesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		562.2	482

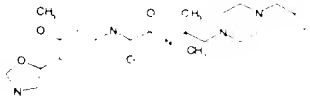
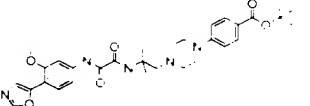
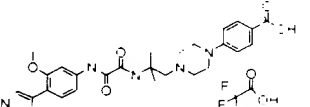
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-phenylethanesulfonyl)-1-piperazinyl]ethyl]oxalamide		570.1	483
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(2,4-dimethoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide		538	484
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(4-methylphenyl)-1-piperazinyl]ethyl]oxalamide		492	485
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2,4-dimethylphenyl)-1-piperazinyl]ethyl]oxalamide		506	486
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(3,4-dimethoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide		538	487
N-[2-(4-Cyclohexyl-1-piperazinyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		484.4	488
N-[2-[4-(Cyclohexylmethyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		498.2	489
N-[2-[4-(2-Methoxybenzyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		522.1	490
N-[2-[4-(2-Hydroxybenzyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		508.1	491
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-methylbenzyl)-1-piperazinyl]ethyl]oxalamide		506.1	492
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-thenyl)-1-piperazinyl]ethyl]oxalamide		498.1	493
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2(RS)-phenylpropyl)-1-piperazinyl]ethyl]oxalamide		520.2	494

N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(4-pivaloyl-1-piperazinyl)ethyl]oxalamide		486.1	495
N-[2-[4-(2-Furoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		496.1	496
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-thenoyl)-1-piperazinyl]ethyl]oxalamide		512.1	497
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(3-thenoyl)-1-piperazinyl]ethyl]oxalamide		512	498
N-[2-[4-(2-Cyclopentylacetyl)-1-piperazinyl]-1,1-dimethyl-ethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		512.1	499
N-[2-[4-(Cyclohexylcarbonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		512.1	500
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-methylbenzoyl)-1-piperazinyl]ethyl]oxalamide		520.1	501
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(4-methylbenzoyl)-1-piperazinyl]ethyl]oxalamide		520.1	502
N-[2-[4-(Cycloheptylcarbonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		526.2	503
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(1H-pyrazol-4-yl)carbonyl]-1-piperazinyl]ethyl]oxalamide		496.1	504
N-[2-[4-(Cyclopentylcarbonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		498.1	505
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-Dimethyl-2-[4-[(1-methyl-1H-pyrrol-2-yl)carbonyl]-1-piperazinyl]ethyl]oxalamide		509.1	506

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(1,2,3-thiadiazol-4-yl)carbonyl]-1-piperazinyl]-ethyl]oxalamide		514.1	507
N-[2-[4-(3-Fluorobenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		524.1	508
N-[2-[4-(4-Fluorobenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		524.1	509
N-[2-[4-(Cyclopropylcarbonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		470.1	510
N-[2-[4-(2-Cyclohexylacetyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		526.2	511
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(3,3-dimethylbutyryl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide		500.2	512
N-[2-[4-(3-Hydroxy-2,2-dimethylpropionyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		502.1	513
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(3-methyl-2-furoyl)-1-piperazinyl]ethyl]oxalamide		510.1	514
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-methyl-3-furoyl)-1-piperazinyl]ethyl]oxalamide		510.1	515
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(5-methyl-1H-pyrazol-3-yl)carbonyl]-1-piperazinyl]ethyl]oxalamide		510.1	516
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(5-methyl-4-isoxazolyl)carbonyl]-1-piperazinyl]ethyl]oxalamide		511.1	517

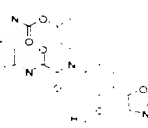
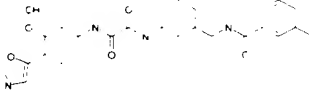
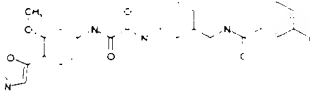
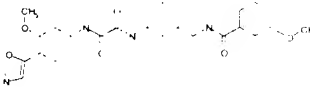

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(5-methyl-3-isoxazolyl)carbonyl]-1-piperazinyl]ethyl]oxalamide		511.1	518
N-[2-[4-(4-Aminobenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		521.1	519
N-[2-[4-(2-Hydroxybenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		522.1	520
N-[2-[4-(4-Hydroxybenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		522.1	521
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(2,5-dimethyl-2H-pyrazol-3-yl)carbonyl]-1-piperazinyl]ethyl]oxalamide		524.1	522
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(3-methyl-2-thenoyl)-1-piperazinyl]ethyl]oxalamide		526.1	523
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(4-methyl-2-thenoyl)-1-piperazinyl]ethyl]oxalamide		526.1	524
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(2,2,3,3-tetramethyl-1-cyclopropyl)carbonyl]-1-piperazinyl]ethyl]oxalamide		526.2	525
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(4-methyl-1,2,3-thiadiazol-5-yl)carbonyl]-1-piperazinyl]ethyl]oxalamide		528.1	526
N-[2-[4-(3-Cyanobenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		531.1	527
N-[2-[4-[(Bicyclo[4.2.0]octa-1(6),2,4-trien-7-yl)carbonyl]-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		532.1	528

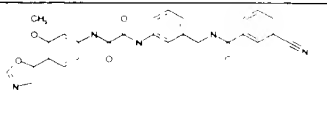
N-[2-[4-(3-Hydroxybenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		522.1	529
N-[2-[4-(2-Ethylbutyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		486.1	530
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-phenylethyl)-1-piperazinyl]ethyl]oxalamide		506.2	531
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[3-(methylthio)propyl]-1-piperazinyl]ethyl]oxalamide		490.1	532
N-[2-[4-(2,6-Difluorobenzyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		528.1	533
N-[2-[4-(3-Furfuryl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		482.1	534
N-[2-[4-[(2-Benzofuranyl)methyl]-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		532.1	535
N-[2-[4-(2-Cyanobenzyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		517.1	536
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(3,3-dimethylbutyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide		486.2	537
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(2-quinolinyl)methyl]-1-piperazinyl]ethyl]oxalamide		543.2	538
tert-Butyl 4-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]-1-piperazineacetate		516	539
4-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]-1-piperazineacetic acid trifluoroacetate (1:1)		460	540

N-[2-[4-(Cyclopropylmethyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		456	541
tert-Butyl 4-[4-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]-1-piperazinyl]benzoate		578	651
4-[4-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]-1-piperazinyl]benzoic acid trifluoroacetate (1:1)		522	652

Examples 415-420:

In a manner analogous to that described in Example 4 starting with N-[3-(aminomethylphenyl)-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide and the appropriate
5 carboxylic acid chloride compounds shown in table 1h were prepared.

table 1h			
Name	Structure	ME(ES) (M+H) ⁺	Ex No
Phenyl [3-[[[4-(5-oxazolyl)anilino]oxalyl]amino]benzyl] carbamate		487	415
N-[3-[(3-Fluorobenzamido)methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		489	416
N-[3-[(3-Chlorobenzamido)methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		505	417
N-[3-[(3-Methoxybenzamido)methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		501.2	418
N-[3-[(3,4-Dimethoxybenzamido)methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		531.2	419

N-[3-[(3-Cyanobenzamido)methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		496.1	420
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Examples 421-427 and 598-614:

Typical methods used for the preparation of the compounds of table 1b are described below:

5 Examples 421 and 423 were prepared by reaction of N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(4-piperidinyl)ethyl]oxalamide with the appropriate acylating reagent.

10 Example 424 was prepared in a manner analogous to that described in Example 1, starting with N-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamic acid, prepared as described in Example 1, parts (i) and (ii), and the appropriate amine.

Example 422

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(phenylthio)ethyl]oxalamide.

15

(i) A mixture of 2g (17.7 mmol) of 2,4,4-trimethyl-2-oxazoline and 1.95 g (17.7 mmol) of thiophenol were heated at 120C for 18 hours. After cooling the resulting solid was triturated with diethyl ether/petrol (1:2) and filtered off to give 2.55 g of N-[1,1-dimethyl-2-(phenylthio)ethyl]acetamide as a white solid.

20

(ii) A solution of 2.5 g (11.2 mmol) of N-[1,1-dimethyl-2-(phenylthio)ethyl]acetamide, 3.18 g (11.2 mmol) of titanium isopropoxide and 3.09 g (16.8 mmol) of diphenylsilane in 12 ml of tetrahydrofuran were stirred at room temperature for 18 hours. The resulting mixture was chromatographed on silica gel using 3%, 6% and 10% methanol in dichloromethane for the
25 elution. There was obtained 2 g of 1,1-dimethyl-2-(phenylthio)ethylamine as a pale orange oil. The 1,1-dimethyl-2-(phenylthio)ethylamine was then coupled to N-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamic acid by a procedure analogous to that described in example 1 to afford N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(phenylthio)ethyl]oxalamide. MS: m/e 426 [M+H]⁺.

30

Example 427 was prepared by an analogous method to that described for example 422 but using 4-benzyloxythiophenol in place of the thiophenol and removing the protecting group using a mixture of hydrogen bromide in acetic acid.

Example 607 was prepared starting from benzofuran-3-acetic ethyl ester by alkylation iodomethane using potassium tertiary butoxide as base followed by alkaline hydrolysis, Curtius reaction, hydrolysis in ethylene glycol and water at 180°C. The resulting amine was then coupled to N-[3-methoxy-4-(5-oxazolyl)phenyl oxalamic acid as described in Example 1.

Example 426 was prepared in a manner analogous to that described for example 408 in table 1g using tetrahydro quinoline in place of 1-(4-methoxyphenyl)piperazine.

Example 610

N-[2-[1-(Methanesulfonyl)-4-piperidinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide

14 mg (0.12 mmol) of methanesulphonyl chloride were added to a solution of 40 mg (0.1 mmol) of N-[3-methoxy-4-(5-oxazolyl)phenyl-N'-[1,1-dimethyl-2-(4-piperidinyl)ethyl]oxalamide in 1 ml of dichloromethane followed by 17 mg (0.15 mmol) of N-ethylmorpholine and the mixture stirred at room temperature for 4 hours. The resulting solution was diluted with ethyl acetate, washed with 2M hydrochloric acid and saturated sodium bicarbonate solution, dried over magnesium sulphate, evaporated to dryness and the residue triturated with diethyl ether. There was obtained 23 mg of N-[2-[1-(methanesulfonyl)-4-piperidinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide as an off-white solid. MS m/e 479 [M+H]⁺.

The starting material was prepared as follows:

i) A solution of 4.65 g (31 mmol) of alpha, alpha-dimethyl-4-pyridineethylamine, 15.6 g (0.154 mol) of triethylamine and 13.5g (61.9 mmol) of di-tert-butyl dicarbonate in 100 ml of methanol was stirred at room temperature for 2 days then evaporated to dryness. The residue

was dissolved in ethyl acetate, washed with water, dried over magnesium sulphate, evaporated to dryness and chromatographed on silica gel using ethyl acetate/petrol (2:1) for the elution. There was obtained 2.12 g of tert-butyl [1,1-dimethyl-2-(4-pyridyl)ethyl]carbamate as a pale orange solid. ¹H NMR (400 MHz CDCl₃) δ: 1.29 (6H,s), 1.49 (9H,s), 3.04 (2H,s), 4.30 (1H, br.s), 7.10 (2H,d), 8.52 (2H,d).

ii) 2.1 g (8.4 mmol) of tert-butyl [1,1-dimethyl-2-(4-pyridyl)ethyl]carbamate, in 20 ml of methanol were hydrogenated with 400 mg of 10% palladium on carbon catalyst at 70°C and 7 Bar for 6 days. The resulting suspension was filtered, evaporated to dryness and the residue triturated with diethyl ether/petrol (1:9) to give 1.2 g of tert-butyl [1,1-dimethyl-2-(4-piperidiny)ethyl]carbamate as a white solid. ¹H NMR (400 MHz DMSO) δ: 1.18 (6H,s), 1.28-1.41 (2H,m), 1.37 (9H,s), 1.52-1.69 (3H,m), 1.75-1.83 (2H,d), 2.74-2.84 (2H,t), 3.12-3.21 (2H,d), 6.40-6.48 (1H,br.s), 8.60-8.95 (1H,br.s).

iii) A solution of 1.2 g (4.68 mmol) of tert-butyl [1,1-dimethyl-2-(4-piperidiny)ethyl]carbamate, 945 mg (9.36 mmol) of triethylamine and 2.33 g (9.36 mmol) of N-(benzyloxycarbonyloxy)succinimide in 20 ml of dichloromethane was stirred at room temperature for 18 hours then washed with 10% citric acid solution and saturated sodium bicarbonate solution. The organic phase was dried over magnesium sulphate, evaporated to dryness and the residue chromatographed on silica gel using ethyl acetate/petrol (1:2) for the elution. There was obtained 1.89 g of benzyl 4-[2-(tert-butoxyformamido)-2-methylpropyl]-1-piperidinecarboxylate. ¹H NMR (400 MHz CDCl₃) δ: 1.15-1.32 (2H,m), 1.29 (6H,s), 1.42 (9H,s), 1.49-1.78 (5H,m), 2.75-2.90 (2H,m), 4.05-4.16 (2H,m), 4.41 (1H,br.s), 5.12 (2H,s), 7.27-7.42 (5H,m).

iv) A solution of 1.79 g (4.6 mmol) of benzyl 4-[2-(tert-butoxyformamido)-2-methylpropyl]-1-piperidinecarboxylate in 6 ml of trifluoroacetic acid/dichloromethane (1:1) was stirred at room temperature for 5 minutes then evaporated to dryness. The residue was dissolved in 20 ml of dichloromethane along with 1.2 g (4.58 mmol) of N-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamic acid, 1.1 g (5.74 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride, 1.32g (11.5 mmol) of N-ethylmorpholine and 1.1 g (6.9mmol) of 1-hydroxy-7-azabenzotriazole. After stirring overnight the solution was diluted with ethyl acetate, washed with 10% citric acid solution and saturated sodium bicarbonate

solution, dried over magnesium sulphate evaporated to dryness and chromatographed on silica gel using ethyl acetate/petrol (1:1) for the elution. There was obtained 1.14 g of benzyl 4-{2-[[[3-methoxy-4-(5-oxazolyl)phenylamino]oxalyl]amino]-2-methylpropyl}-1-piperidinecarboxylate as a white foam. MS: m/e 535 [M+H]⁺.

5

v) A solution of 1.1 g (2.05 mmol) of benzyl 4-{2-[[[3-methoxy-4-(5-oxazolyl)phenylamino]oxalyl]amino]-2-methylpropyl}-1-piperidinecarboxylate in 25 ml of methanol was hydrogenated with 100 mg of 10% palladium on carbon catalyst for 4 hours. The resulting suspension was filtered and evaporated to dryness to give 732 mg of N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(4-piperidinyl)ethyl]oxalamide as an off-white solid. MS: m/e 401 [M+H]⁺.

Example 616 was prepared starting from benzofuran-3-acetic ethyl ester by alkylation iodomethane using potassium tertiary butoxide as base followed by alkaline hydrolysis, Curtius reaction, hydrolysis in ethylene glycol and water at 180°C. The resulting amine was then coupled to N-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamic acid as described in Example 1

Example 619

20 N-[2-[1-(Methanesulfonyl)-4-piperidinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide

14 mg (0.12 mmol) of methanesulphonyl chloride were added to a solution of 40 mg (0.1 mmol) of N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(4-piperidinyl)ethyl]oxalamide in 1 ml of dichloromethane followed by 17 mg (0.15 mmol) of N-ethylmorpholine and the mixture stirred at room temperature for 4 hours. The resulting solution was diluted with ethyl acetate, washed with 2M hydrochloric acid and saturated sodium bicarbonate solution, dried over magnesium sulphate, evaporated to dryness and the residue triturated with diethyl ether. There was obtained 23 mg of N-[2-[1-(methanesulfonyl)-4-piperidinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide as an off-white solid. MS m/e 479 [M+H]⁺.

The starting material was prepared as follows:

- i) A solution of 4.65 g (31 mmol) of alpha, alpha-dimethyl-4-pyridineethylamine, 15.6 g (0.154 mol) of triethylamine and 13.5g (61.9 mmol) of di-tert-butyl dicarbonate in 100 ml of methanol was stirred at room temperature for 2 days then evaporated to dryness. The residue was dissolved in ethyl acetate, washed with water, dried over magnesium sulphate, evaporated to dryness and chromatographed on silica gel using ethyl acetate/petrol (2:1) for the elution. There was obtained 2.12 g of tert-butyl [1,1-dimethyl-2-(4-pyridyl)ethyl]carbamate as a pale orange solid. ¹H NMR (400 MHz CDCl₃) δ: 1.29 (6H,s), 1.49 (9H,s), 3.04 (2H,s), 4.30 (1H, br.s), 7.10 (2H,d), 8.52 (2H,d).
- 10 ii) 2.1 g (8.4 mmol) of tert-butyl [1,1-dimethyl-2-(4-pyridyl)ethyl]carbamate, in 20 ml of methanol were hydrogenated with 400 mg of 10% palladium on carbon catalyst at 70°C and 7 Bar for 6 days. The resulting suspension was filtered, evaporated to dryness and the residue triturated with diethyl ether/petrol (1:9) to give 1.2 g of tert-butyl [1,1-dimethyl-2-(4-piperidinyl)ethyl]carbamate as a white solid. ¹H NMR (400 MHz DMSO) δ: 1.18 (6H,s), 1.28-1.41 (2H,m), 1.37 (9H,s), 1.52-1.69 (3H,m), 1.75-1.83 (2H,d), 2.74-2.84 (2H,t), 3.12-3.21 (2H,d), 6.40-6.48 (1H,br.s), 8.60-8.95 (1H,br.s).
- 15 iii) A solution of 1.2 g (4.68 mmol) of tert-butyl [1,1-dimethyl-2-(4-piperidinyl)ethyl]carbamate, 945 mg (9.36 mmol) of triethylamine and 2.33 g (9.36 mmol) of N-(benzyloxycarbonyloxy)succinimide in 20 ml of dichloromethane was stirred at room temperature for 18 hours then washed with 10% citric acid solution and saturated sodium bicarbonate solution. The organic phase was dried over magnesium sulphate, evaporated to dryness and the residue chromatographed on silica gel using ethyl acetate/petrol (1:2) for the elution. There was obtained 1.89 g of benzyl 4-[2-(tert-butoxyformamido)-2-methylpropyl]-1-piperidinecarboxylate. ¹H NMR (400 MHz CDCl₃) δ: 1.15-1.32 (2H,m), 1.29 (6H,s), 1.42 (9H,s), 1.49-1.78 (5H,m), 2.75-2.90 (2H,m), 4.05-4.16 (2H,m), 4.41 (1H,br.s), 5.12 (2H,s), 7.27-7.42 (5H,m).
- 20 iv) A solution of 1.79 g (4.6 mmol) of benzyl 4-[2-(tert-butoxyformamido)-2-methylpropyl]-1-piperidinecarboxylate in 6 ml of trifluoroacetic acid/dichloromethane (1:1) was stirred at room temperature for 5 minutes then evaporated to dryness. The residue was dissolved in 20 ml of dichloromethane along with 1.2 g (4.58 mmol) of N-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamic acid, 1.1 g (5.74 mmol) of 1-(3-dimethylaminopropyl)-3-

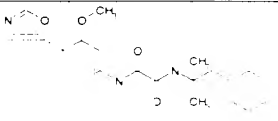
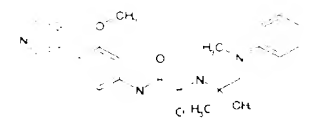
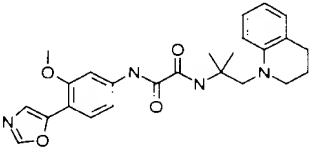
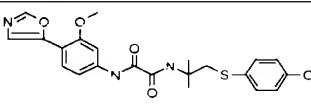
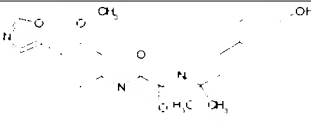
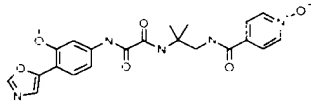
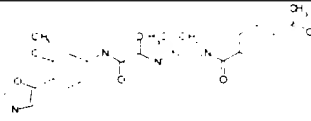

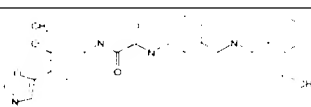
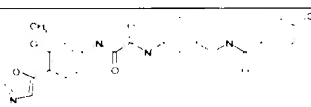
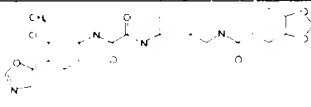
ethylcarbodiimide hydrochloride, 1.32g (11.5 mmol) of N-ethylmorpholine and 1.1 g (6.9mmol) of 1-hydroxy-7-azabenzotriazole. After stirring overnight the solution was diluted with ethyl acetate, washed with 10% citric acid solution and saturated sodium bicarbonate solution, dried over magnesium sulphate evaporated to dryness and chromatographed on silica gel using ethyl acetate/petrol (1:1) for the elution. There was obtained 1.14 g of benzyl 4-{2-[[[3-methoxy-4-(5-oxazolyl)phenylamino]oxalyl]amino]-2-methylpropyl}-1-piperidinecarboxylate as a white foam. MS: m/e 535 [M+H]⁺.

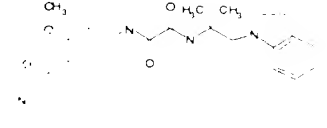
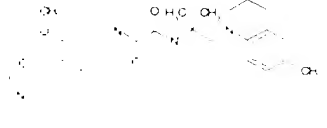
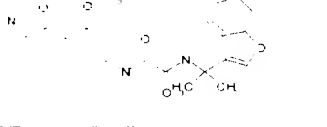
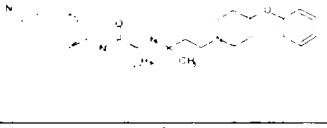
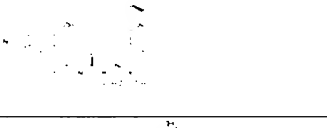
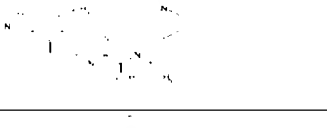
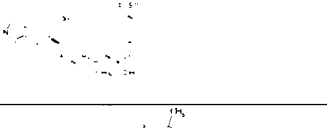
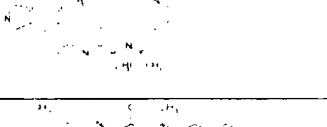
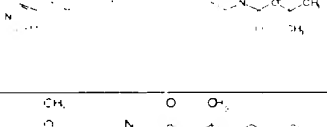

v) A solution of 1.1 g (2.05 mmol) of benzyl 4-{2-[[[3-methoxy-4-(5-oxazolyl)phenylamino]oxalyl]amino]-2-methylpropyl}-1-piperidinecarboxylate in 25 ml of methanol was hydrogenated with 100 mg of 10% palladium on carbon catalyst for 4 hours. The resulting suspension was filtered and evaporated to dryness to give 732 mg of N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(4-piperidinyl)ethyl]oxalamide as an off-white solid. MS: m/e 401 [M+H]⁺.

The remaining examples in table 1b were prepared by methods analogous to those described above, as appropriate to the structure, or by methods previously described for related structures.

table 1b

Name	Structure	MS(ES) (M+H) ⁺	Ex No
Benzyl 4-{2-[[[3-methoxy-4-(5-oxazolyl)phenylamino]oxalyl]amino]-2-methylpropyl}-1-piperidinecarboxylate		535	421
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(phenylthio)ethyl]oxalamide		426	422
N-[2-(1-Acetyl-4-piperidinyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		443	423

N-(2-Cyclohexyl-1,1-dimethylethyl)-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		400	424
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(N-methylanilino)ethyl]oxalamide		423	425
N-[2-(1,2,3,4-Tetrahydro-1-quinolyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		449	426
N-[2-(4-Hydroxyphenylthio)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		442	427
N-[3-(4-Hydroxyphenyl)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		424	598
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[(1-oxido-4-pyridyl)carboxamido]ethyl]oxalamide		454	599
N-[2-(4-Acetylbenzamido)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		479.1	600
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[3-[(4-methylbenzamido)methyl]phenyl]oxalamide		485.1	601
N-[3-[(2-Methoxybenzamido)methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		501.1	602
N-[3-[(4-Chlorobenzamido)methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		505.1	603
N-[3-[[1,3-Benzodioxol-5-yl]carboxamido]methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		515.2	604

N-[2-(2,3-Dihydro-1-indolyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		435	605
N-[2-(3,4-Dihydro-6-methyl-2H-quinol-1-yl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		463	606
N-[1-(3-Benzofuranyl)-1-methylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		420	607
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(4-phenoxy-piperidino)propyl]oxalamide		507	608
N-[2-(1-Butyryl-4-piperidiny)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		471	609
N-[2-[1-(Methanesulfonyl)-4-piperidiny]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		479	610
N-[2-[1-(Benzenesulfonyl)-4-piperidiny]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		541	611
N-[2-(1-Isobutyryl-4-piperidiny)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide		471	612
tert-Butyl 4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino] oxalyl]amino]-3-methylbutyl]-1-piperidinecarboxylate		515	613
N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(4-piperidiny)propyl]oxalamide		415	614

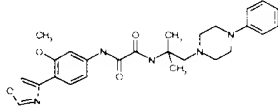
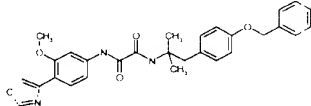
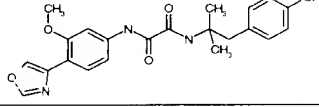
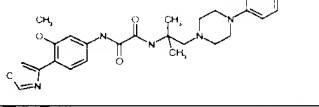
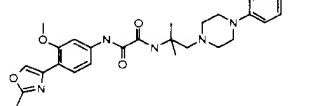
Examples 428-432:

Examples 428, 431 and 432 of table 1i were prepared in a manner analogous to that described for example 408 in table 1g but using N-[3-methoxy-4-(4-oxazolyl)phenyl oxalamic acid or N-[3-methoxy-4-(2-methyl-4-oxazolyl)phenyl oxalamic acid in place of N-[3-methoxy-4-(5-oxazolyl)phenyl oxalamic acid for the coupling step.

Examples 429 and 430 of table 1i were prepared by analogous procedures to those described for the preparation of the compounds of table 1f.

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table 1i

Name	Structure	MS(ES) (M+H) ⁺	Ex No
N-[3-Methoxy-4-(4-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(4-phenyl-1-piperazinyl)ethyl]oxalamide		478	428
N-[2-(4-Benzyloxyphenyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(4-oxazolyl)phenyl]oxalamide		500	429
N-[2-(4-Hydroxyphenyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(4-oxazolyl)phenyl]oxalamide		410	430
N-[3-Methoxy-4-(4-oxazolyl)phenyl]-N'-[2-[4-(4-methoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide		508	431
N-[3-Methoxy-4-(2-methyl-4-oxazolyl)-phenyl]-N'-[2-[4-(4-methoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide		522.4	432

The features disclosed in the foregoing description, or the following claims, or the accompanying drawings, expressed in their specific forms or in terms of a means for performing the disclosed function, or a method or process for attaining the disclosed result, as appropriate, may, separately, or in any combination of such features, be utilised for realising the invention in diverse forms thereof.

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